

PATENT

Continuation-in-Part Application Transmittal  
Under Rule 1.53(b)

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Docket Number	Anticipated Classification of this Application	Prior Application Serial Number: 09/322,409	Prior Application Filing date: May 28, 1999
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ASSISTANT COMMISSIONER FOR PATENTS  
BOX PATENT APPLICATIONS  
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CERTIFICATION UNDER 37 CFR 1.10

Date of Deposit: December 1, 1999 Mailing Label Number: EL344800881US

I hereby certify that this 37 CFR 1.53(b) request and the documents referred to as attached therein are being deposited with the United States Postal Service on the date indicated above in an envelope as "Express Mail Post Office to Addressee" service under 37 CFR 1.10 and addressed to the Assistant Commissioner for Patents, Box Patent Application, Washington, DC 20231.

Susan Gordon  
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*Susan Gordon*  
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Dear Sir:

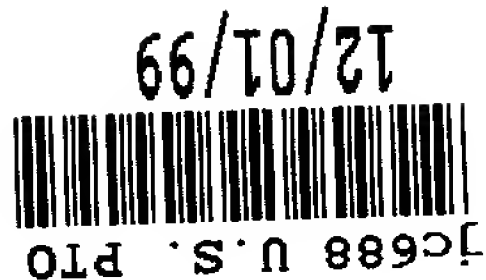
This is a request for filing a continuation-in-part application under 37 CFR 1.53(b) of prior pending U.S. Patent Application Serial No. 09/322,409, filed May 28, 1999, entitled "CANINE AND FELINE IMMUNOREGULATORY PROTEINS, NUCLEIC ACID MOLECULES, AND USES THEREOF"; which claims priority to U.S. Provisional Patent Application Serial No. 60/087,306, filed May 29, 1998, entitled "CANINE INTERLEUKIN-4 AND FLT-3 LIGAND PROTEINS, NUCLEIC ACID MOLECULES, AND USES THEREOF".

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FOR: "CANINE AND FELINE IMMUNOREGULATORY PROTEINS, NUCLEIC ACID MOLECULES, AND USES THEREOF"

ENCLOSED ARE:

- ☒ 227 PAGES OF SPECIFICATION, CLAIMS AND ABSTRACT
- ☐ \_\_\_\_\_ SHEETS OF DRAWING ([ ] FORMAL OR [ ] INFORMAL)
- ☐ DECLARATION
- ☐ POWER OF ATTORNEY
- ☐ ASSIGNMENT OF THE INVENTION TO: [Heska Corporation] (Under separate cover letter)
- ☒ IDENTICAL PAPER AND COMPUTER READABLE FORMS OF THE SEQUENCE LISTING. APPLICANT HEREBY ASSERTS PURSUANT TO 37 CFR §1.821(f) THAT THE CONTENT OF THE PAPER AND COMPUTER READABLE FORMS OF SEQ ID NO:1 THROUGH SEQ ID NO:174 SUBMITTED HERewith ARE IDENTICAL.
- ☐ FOREIGN PRIORITY BENEFITS ARE CLAIMED UNDER 35 USC §119 OF \_\_\_\_\_ (Country) PATENT APPLICATION SERIAL NO. \_\_\_\_\_, FILED \_\_\_\_\_.
- ☐ CERTIFIED COPY OF A \_\_\_\_\_ APPLICATION.
- ☒ FILING FEE IS NOT ENCLOSED AT THIS TIME.



- ☐ ENCLOSED IS A CHECK IN THE AMOUNT OF \$\_\_\_\_\_ TO COVER THE FILING FEE. SEE FOLLOWING PAGE FOR CALCULATION OF FILING FEE.
- ☐ THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE PAYMENT OF THE FOLLOWING FEES ASSOCIATED WITH THIS COMMUNICATION OR CREDIT ANY OVERPAYMENT TO DEPOSIT ACCOUNT NO. 081930. A DUPLICATE COPY OF THIS SHEET IS ENCLOSED.
- ☐ ANY ADDITIONAL FILING FEES REQUIRED UNDER 37 C.F.R. 1.16.
- ☐ ANY PATENT APPLICATION PROCESSING FEES UNDER 37 C.F.R. 1.17.
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- ☐ ANY PATENT APPLICATION PROCESSING FEES UNDER 37 C.F.R. 1.17.
- ☐ THE ISSUE FEE SET IN 37 C.F.R. 1.18 AT OR BEFORE MAILING OF THE NOTICE OF ALLOWANCE, PURSUANT TO 37 C.F.R. 1.31(b).
- ☐ ANY FILING FEES UNDER 37 C.F.R. 1.16 FOR PRESENTATION OF EXTRA CLAIMS.

THE FILING FEE HAS BEEN CALCULATED AS SHOW BELOW:

	(COL. 1) NO. FILED			(COL. 2*) NO. EXTRA	SMALL ENTITY			LARGE ENTITY	
					RATE	FEE		RATE	FEE
BASIC FEE:						\$380.00	OR		\$760.00
TOTAL CLAIMS:	32	-	20	12	X \$9 =	\$	OR	X \$18 =	\$216.00
INDEP. CLAIMS:	9	-	3	6	X \$39 =	\$	OR	X \$78 =	\$468.00
____ MULTIPLE DEPENDENT CLAIMS					+ \$130 =		OR	+\$260 =	\$
*IF THE DIFFERENCE IN COL. 2 IS LESS THAN ZERO, ENTER "O" IN COL. 2.					TOTAL:	\$			\$1444.00

- ☒ THE COMMISSIONER IS HEREBY AUTHORIZED TO SUBMIT ALL CORRESPONDENCE RELATING TO THIS CASE TO THE CORRESPONDENCE ADDRESS LISTED BELOW.

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Date: December 1, 1999

**CORRESPONDENCE ADDRESS:**

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# CANINE AND FELINE IMMUNOREGULATORY PROTEINS, NUCLEIC ACID MOLECULES, AND USES THEREOF

## CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority to pending U.S. Patent Application Serial  
5 No. 09/322,409, filed May 28, 1999, entitled "CANINE AND FELINE  
IMMUNOREGULATORY PROTEINS, NUCLEIC ACID MOLECULES, AND USES  
THEREOF"; which claims priority to U.S. Provisional Patent Application Serial  
No. 60/087,306, filed May 29, 1998, entitled "CANINE INTERLEUKIN-4 AND FLT-3  
LIGAND PROTEINS, NUCLEIC ACID MOLECULES, AND USES THEREOF"; each  
10 of which is incorporated herein by reference in its entirety.

## FIELD OF THE INVENTION

The present invention relates to canine interleukin-4, canine or feline Flt-3 ligand,  
canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-  
13, feline interferon alpha, or feline GM-CSF nucleic acid molecules, proteins encoded  
15 by such nucleic acid molecules, antibodies raised against such proteins and/or inhibitors  
of such proteins or nucleic acid molecules. The present invention also includes  
therapeutic compositions comprising such nucleic acid molecules, proteins, antibodies  
and/or inhibitors, as well as their use to regulate an immune response in an animal.

## BACKGROUND OF THE INVENTION

20 Regulating immune responses in animals is important in disease management.  
Immune responses can be regulated by modifying the activity of immunoregulatory  
molecules and immune cells.

Several immunoregulatory molecules have been found in humans and other mammal species. Interleukin-4, produced by activated type 2 helper cells ( $T_H2$  cells), has a number of functions. These functions include promotion of naive T cells and B cells to differentiate and proliferate. IL-4 promotes  $T_H2$  differentiation and inhibits  $T_H1$  development. FMS-like tyrosine kinase 3, (Flt-3 ligand) stimulates the expansion and mobilization of hematopoietic precursor cell stimulating activity. CD40 is a type I transmembrane protein expressed on antigen presenting cells, such as B lymphocytes, and other types of cells such as endothelial cells, epithelial cells, and fibroblasts. CD40 ligand (also known as CD154) is a type II transmembrane protein that is preferentially expressed on activated T lymphocytes. The CD40-CD154 interaction regulates diverse pathways of the immune system, including B cell proliferation, immunoglobulin production and class switching by B cells, activation and clonal expansion of T cells, activity of antigen presenting cells, growth and differentiation of epithelial cells, and regulation of inflammatory responses at mucosal and cutaneous sites. Interleukin-5 is produced by activated type 2 helper cells ( $T_H2$ ), mast cells, and eosinophils. Its main functions include promotion of growth and differentiation of eosinophils and generation of cytotoxic T cells from thymocytes. Interleukin-13 is produced by  $T_H1$  and  $T_H2$  cells, and promotes growth and differentiation of B cells, up-regulation of MHC class II and CD23 expression on monocytes/macrophages and B cells; and inhibition of production of inflammatory cytokines such as IL-1 $\alpha$ , IL-1 $\beta$ , IL-6, IL-8, IL-10, IL-12, among others. Interferon alpha is an antiviral protein that has three major functions: it inhibits viral replication by activating cellular genes that destroy mRNA and inhibit protein translation, it induces MHC class I expression in non virally-infected cells, increasing resistance to



NK cells, and can activate NK cells. GM-CSF, (granulocyte-macrophage colony-stimulating factor) stimulates the production of granulocytes and macrophages.

Prior investigators have disclosed sequences encoding feline IL-4 (Lerner et al., Genbank Accession No. U39634); porcine IL-4 (Zhou et al., Genbank Accession No. L12991); bovine IL-4 (Heussler, V.T., et al., *Gene*, vol. 114, pp. 273-278, 1992); ovine IL-4 (Seow, H.-F., et al., *Gene*, vol. 124, pp. 291-293, 1993); human IL-4 (Yokota, T., et al., *Proc. Natl. Acad. Sci. U.S.A.*, vol. 83(16), pp. 5894-5898, 1986); and murine IL-4 (Sideras, P., et al., *Adv. Exp. Med. Biol.*, vol. 213, pp. 227-236, 1987). Prior investigators have disclosed sequences encoding murine Flt-3 ligand (McClanahan et al., Genbank Accession No. U44024); and human Flt-3 ligand (Lyman et al., *Blood*, vol. 83, pp. 2795-2801, 1994). Prior investigators have disclosed sequences encoding human CD40 (Stamenkovic et al., *EMBO J.*, vol. 8:1403-1410, 1989, GenBank Accession No. X60592), bovine CD40 (Hirano et al., *Immunology*, vol. 90, pp. 294-300, 1997, GenBank Accession No. U57745), and murine CD40 (Grimaldi et al., *J. Immunol.*, vol. 143, pp.3921-3926, 1992; Torres and Clark, *J. Immunol.*, vol. 148, pp. 620-626, 1992, GenBank Accession No. M83312). Prior investigators have disclosed sequences encoding human CD154 (Graf et al., *Eur. J. Immunol.*, vol. 22, pp. 3191-3194, 1992; Hollenbaugh, et al., *EMBO J.*, vol. 11:4313-4321, 1992; Gauchat et al., *FEBS lett.*, vol. 315, pp. 259-266, 1993; GenBank Accession Nos L07414, X68550, Z15017, X67878, respectively); bovine CD154 (Mertens et al., *Immunogenetics*, vol. 42, pp. 430-431, GenBank Accession No. Z48468); and murine CD154 (Armitage et al., *Nature*, vol. 357, pp. 80-82; 1992, GenBank Accession No. X65453). Prior investigators have disclosed sequences encoding feline interleukin-5 (Padrid et al., *Am. J. Vet. Res.*, vol. 59, pp. 1263-

1269, 1998, GenBank Accession No. AF025436) and human interleukin-5 (Azuma et al.,  
*Nucleic Acids Res.*, vol. 14, pp. 9149-9158, 1986, GenBank Accession No. X04688).

Prior investigators have disclosed sequences encoding human interleukin-13 (McKenzie  
 et al., *Proc. Natl Acad. Sci. USA*, vol. 90, pp. 3735-3739, 1993; Minty et al., *Nature*, vol.

- 5 362, pp. 248-250, 1993, GenBank Accession Nos L06801 and X69079, respectively);  
 murine interleukin-13 (Brown et al., *J. Immunol.*, vol. 142, pp. 679-687, 1989, GenBank  
 Accession No M23504); and rat interleukin-13 (Lakkis et al., *Biochem. Biophys. Res.*  
*Commun.*, Vol. 197, pp. 612-618, 1993, GenBank Accession No. L26913). Prior  
 investigators have disclosed sequences encoding feline interferon (Nakamura, N., Sudo,  
 10 T., Matsuda, S., Yanai, A., *Biosci. Biotechnol. Biochem.* (1992)Vol: 56 pp 211-214,  
 GenBank accession # E02521). Prior investigators have also disclosed sequences  
 encoding feline GM-CSF (direct submission to GenBank, Accession No. AF053007)

- There remains a need for compounds and methods to regulate an immune  
 response by manipulation of the function of canine interleukin-4, canine or feline Flt-3  
 15 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine  
 interleukin-13, feline interferon alpha, or feline GM-CSF.

#### SUMMARY OF THE INVENTION

- The present invention relates to canine interleukin-4, canine or feline Flt-3 ligand,  
 canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-  
 20 13, feline interferon alpha, or feline GM-CSF nucleic acid molecules, proteins encoded  
 by such nucleic acid molecules, antibodies raised against such proteins and/or inhibitors  
 of such proteins or nucleic acid molecules. Identification of the nucleic acid molecules of  
 the present invention is unexpected because initial attempts to obtain nucleic acid

molecules using PCR were unsuccessful. After numerous attempts, the inventors discovered specific primers that were useful for isolating such nucleic acid molecules.

One embodiment of the present invention is an isolated nucleic acid molecule selected from the group consisting of: (a) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21 or a homolog thereof, wherein said homolog has an at least about 50 contiguous nucleotide region identical in sequence to a 50 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21; (b) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37 or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a 40 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37; (c) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or SEQ ID NO:50, and/or a

homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or SEQ ID NO:50; (d) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or SEQ ID NO:59, and/or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a 40 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or SEQ ID NO:59; (e) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and/or SEQ ID NO:62, and/or a homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and/or SEQ ID NO:62; (f) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69 and/or SEQ ID NO:71, and/or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID

NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69 and/or SEQ ID NO:71; (g) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79, and/or a homolog thereof, wherein said

5 homolog has an at least 35 contiguous nucleotide region identical in sequence to a 35 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79; (h) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ

10 ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and/or SEQ ID NO:87, and/or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and/or SEQ

15 ID NO:87; (i) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106, and/or a homolog thereof, wherein said homolog has an

20 at least 15 contiguous nucleotide region identical to a 15 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93,

SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106; (j) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:172; and/or (k) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:126.

Another embodiment of the present invention is an isolated nucleic acid molecule selected from the group consisting of: (a) a nucleic acid molecule having a nucleic acid sequence that is at least about 92 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21; (b) a nucleic acid molecule having a nucleic acid sequence that is at least about 75 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37; (c) a nucleic acid molecule having a nucleic acid sequence that is at least about 75 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43,



SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or SEQ ID NO:50;

(d) a nucleic acid molecule having a nucleic acid sequence that is at least about 70 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or SEQ ID NO:59; (e) a nucleic acid molecule having a nucleic acid sequence that is at least about 70 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and/or SEQ ID NO:62; (f) a nucleic acid molecule having a nucleic acid sequence that is at least about 85 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, and/or SEQ ID NO:71; (g) a nucleic acid molecule having a nucleic acid sequence that is at least about 91 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79; (h) a nucleic acid molecule having a nucleic acid sequence that is at least about 90 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and/or SEQ ID NO:87; (i) a nucleic acid molecule having a nucleic acid sequence that is at least about 65 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106; (j) a nucleic acid molecule having a nucleic acid sequence that is

selected from the group consisting of SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170 and/or SEQ ID NO:172; and/or (k) a nucleic acid molecule having a nucleic acid sequence that is selected from the group consisting of SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, and/or SEQ ID NO:126.

Yet another embodiment of the present invention is an isolated nucleic acid molecule selected from the group consisting of: (a) a nucleic acid molecule having a nucleic acid sequence encoding an IL-4 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20 and/or (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20; (b) a nucleic acid molecule having a nucleic acid sequence encoding a Flt-3 ligand protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34 and/or (ii) a protein comprising a fragment of at least 25 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34; (c) a nucleic

acid molecule having a nucleic acid sequence encoding a Flt-3 ligand protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:44 and/or SEQ ID NO:49 and/or (ii) a protein comprising a fragment of at least 25 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:44 and/or SEQ ID NO:49;

(d) a nucleic acid molecule having a nucleic acid sequence encoding a CD40 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:53 and/or SEQ ID NO:58 and/or (ii) a protein comprising a fragment of at least 30 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:53 and/or SEQ ID NO:58; (e) a nucleic acid molecule having a nucleic acid sequence encoding a CD40 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 60 percent identical to an amino acid sequence comprising SEQ ID NO:61 and/or (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence comprising SEQ ID NO:61; (f) a nucleic acid molecule having a nucleic acid sequence encoding a CD154 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 80 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:65 and/or SEQ ID NO:70, and/or (ii) a protein comprising a fragment of at least 35 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:65 and/or SEQ ID NO:70; (g) a nucleic acid molecule having a nucleic acid sequence encoding a CD154 protein selected from the

group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:73 and/or SEQ ID NO:78, and/or (ii) a protein comprising a fragment of at least 50 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:73 and/or SEQ ID NO:78; (h) a nucleic acid molecule having a nucleic acid sequence encoding an IL-5 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86 and/or (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86; (i) a nucleic acid molecule having a nucleic acid sequence encoding an IL-13 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105 and/or (ii) a protein comprising a fragment of at least 15 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105; (j) a nucleic acid molecule having a nucleic acid sequence encoding an interferon alpha protein having an amino acid sequence that is selected from the group consisting of amino acid sequence SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and/or SEQ ID NO:171; (k) a nucleic acid molecule having a nucleic acid sequence encoding a GMCSF protein having an amino acid sequence that is selected from the group consisting of amino acid sequence SEQ ID NO:120, SEQ ID NO:125,

and/or (l) a nucleic acid molecule comprising a complement of any of said nucleic acid molecules as set forth in (a), (b), (c), (d), (e), (f), (g), (h), (i), (j), and/or (k), wherein said IL-4 protein elicits an immune response against an IL-4 protein selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20 and/or is a protein with interleukin-4 activity, said Flt-3 ligand protein elicits an immune response against a Flt-3 ligand protein selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:44, and/or SEQ ID NO:49 and/or is a protein with Flt-3 ligand activity, said CD40 protein elicits an immune response against a CD40 protein selected from the group consisting of SEQ ID NO:53, SEQ ID NO:58, and/or SEQ ID NO:61 and/or is a protein with CD40 activity, said CD154 protein elicits an immune response against a CD154 protein selected from the group consisting of SEQ ID NO:65, SEQ ID NO:70, SEQ ID NO:73, and/or SEQ ID NO:78 and/or is a protein with CD154 activity, said IL-5 protein elicits an immune response against a IL-5 protein selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86 and/or is a protein with IL-5 activity, said IL-13 protein elicits an immune response against an IL-13 protein selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105 and/or is a protein with IL-13 activity, said interferon alpha protein elicits an immune response against an interferon alpha protein selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and/or SEQ ID NO:171 and/or is a protein with interferon alpha activity, and/or said GMCSF protein elicits an immune response against a GMCSF protein selected from

the group consisting of SEQ ID NO:120 and/or SEQ ID NO:125 and/or is a protein with GM-CSF activity.

The present invention also includes methods to produce any of the proteins of the present invention using nucleic acid molecules of the present invention and  
 5 recombinantly using such nucleic acid molecules.

The present invention also includes an isolated protein selected from the group consisting of: (a) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous  
 10 nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:4, and/or SEQ ID NO:19; and/or (ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20, wherein said isolated protein  
 15 elicits an immune response against a canine IL-4 protein and/or has IL-4 activity; (b) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID  
 20 NO:9, SEQ ID NO:22, SEQ ID NO:25, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:33, and/or SEQ ID NO:36; and/or (ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of



SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34, wherein said isolated protein is capable of eliciting an immune response against a canine Flt-3 ligand protein and/or has Flt-3 activity; (c) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule,

5 wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:46, and/or SEQ ID NO:48; and/or (ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid

10 region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:44 and/or SEQ ID NO:49, wherein said isolated protein is capable of eliciting an immune response against a feline Flt-3 ligand protein and/or has Flt-3 activity; (d)(i) an isolated protein of at least about 30 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule

15 has an at least 90 contiguous nucleotide region identical in sequence to a 90 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, and/or SEQ ID NO:57; and/or (ii) an isolated protein of at least about 30 amino acids in length, wherein said protein has an at least 30 contiguous amino acid region identical in sequence to a 30 contiguous amino acid region

20 selected from the group consisting of SEQ ID NO:53, SEQ ID NO:58, wherein said isolated protein is capable of eliciting an immune response against a canine CD40 protein and/or has CD40 activity; (e) (i) an isolated protein of at least about 20 amino acids in

length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence comprising **SEQ ID NO:60**; and/or (ii) an isolated protein of at least about 20 amino acids in length, wherein said

5 protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region comprising the amino acid sequence **SEQ ID NO:61**, wherein said isolated protein is capable of eliciting an immune response against a feline CD40 protein and/or has CD40 activity; (f)(i) an isolated protein of at least about 35 amino acids in length, wherein said protein is encoded by a nucleic acid molecule,

10 wherein said nucleic acid molecule has an at least 105 contiguous nucleotide region identical in sequence to a 105 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of **SEQ ID NO:63**, **SEQ ID NO:64**, **SEQ ID NO:67**, and/or **SEQ ID NO:69**; and/or (ii) an isolated protein of at least about 35 amino acids in length, wherein said protein has an at least 35 contiguous amino acid region identical in

15 sequence to a 35 contiguous amino acid region selected from the group consisting of **SEQ ID NO:65** and/or **SEQ ID NO:70**, wherein said isolated protein is capable of eliciting an immune response against a canine CD154 protein and/or has CD154 activity; (g)(i) an isolated protein of at least about 50 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at

20 least 150 contiguous nucleotide region identical in sequence to a 150 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of **SEQ ID NO:72**, **SEQ ID NO:75**, and/or **SEQ ID NO:77**; and/or (ii) an isolated protein of at

least about 50 amino acids in length, wherein said protein has an at least 50 contiguous amino acid region identical in sequence to a 50 contiguous amino acid region selected from the group consisting of SEQ ID NO:73 and/or SEQ ID NO:78, wherein said isolated protein is capable of eliciting an immune response against a feline CD154 protein

5 and/or has CD154 activity; (h)(i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:83, and/or SEQ ID NO:85; and/or (ii) an

10 isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86, wherein said isolated protein is capable of eliciting an immune response against a canine IL-5 protein and/or has IL-5 activity; (i)(i) an isolated protein of at least about 15 amino

15 acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, and/or SEQ ID NO:104;

20 and/or (ii) an isolated protein of at least about 15 amino acids in length, wherein said protein has an at least 15 contiguous amino acid region identical in sequence to a 15 contiguous amino acid region selected from the group consisting of SEQ ID NO:92, SEQ

ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105, wherein said isolated protein is capable of eliciting an immune response against a canine IL-13 protein and/or has IL-13 activity; (j) (i) an isolated protein encoded by a nucleic acid molecule selected from the group consisting of SEQ ID NO:107, SEQ ID NO:110, SEQ ID NO:113, SEQ ID NO:116, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:161, SEQ ID NO:164, SEQ ID NO:167, and/or SEQ ID NO:170, and/or (ii) an isolated protein selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and/or SEQ ID NO:171, wherein said isolated protein is capable of eliciting an immune response against a feline interferon alpha protein and/or has interferon alpha activity; (k) (i) an isolated protein encoded by a nucleic acid molecule selected from the group consisting of SEQ ID NO:119, SEQ ID NO:122, and/or SEQ ID NO:124, and/or (ii) an isolated protein selected from the group consisting of SEQ ID NO:120 and/or SEQ ID NO:125, wherein said isolated protein is capable of eliciting an immune response against a feline GM-CSF and/or has GM-CSF activity.

The present invention also includes an isolated protein selected from the group consisting of: (a) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20; (b) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34; (c) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:44

and/or SEQ ID NO:49; (d) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:53 and/or SEQ ID NO:58; (e) a protein having an amino acid sequence that is at least about 60 percent identical to an amino acid sequence comprising SEQ ID NO:61;

5 (f) a protein having an amino acid sequence that is at least about 80 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:65 and/or SEQ ID NO:70; (g) a protein having an amino acid sequence that is at least about 85 percent identical to the amino acid sequence SEQ ID NO:73 and/or SEQ ID NO:78; (h) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid

10 sequence selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86; (i) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105; (j) a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ

15 ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and/or SEQ ID NO:171; and/or (k) a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:120, and/or SEQ ID NO:125.

The present invention also includes isolated antibodies that selectively bind to a

20 protein of the present invention.

One aspect of the present invention is a therapeutic composition that, when administered to an animal, regulates an immune response in said animal, said therapeutic composition comprising a therapeutic compound selected from the group consisting of:

an immunoregulatory protein of the present invention; a mimetope of any of said immunoregulatory proteins; and a multimeric form of any of said immunoregulatory proteins; an isolated nucleic acid molecule of the present invention; an antibody that selectively binds to any of said immunoregulatory proteins; and/or an inhibitor of a  
5 immunoregulatory protein activity identified by its ability to inhibit the activity of any of said immunoregulatory proteins. Yet another aspect of the present invention is a method to regulate an immune response in an animal comprising administering to the animal a therapeutic composition of the present invention.

The present invention also includes a method to produce an immunoregulatory  
10 protein, said method comprising culturing a cell capable of expressing said protein, said protein being encoded by a nucleic acid molecule of the present invention.

One embodiment of the present invention is a method to identify a compound capable of regulating an immune response in an animal, said method comprising: (a) contacting an isolated canine IL-4 protein of the present invention with a putative  
15 inhibitory compound under conditions in which, in the absence of said compound, said protein has T cell proliferation stimulating activity; and determining if said putative inhibitory compound inhibits said activity; (b) contacting an isolated canine Flt-3 ligand protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has dendritic precursor cell  
20 proliferation stimulating activity; and determining if said putative inhibitory compound inhibits said activity; (c) contacting an isolated feline Flt-3 ligand protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has dendritic precursor cell proliferation stimulating



activity; and determining if said putative inhibitory compound inhibits said activity; (d) contacting an isolated canine CD40 protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has CD40 ligand binding activity; and determining if said putative inhibitory compound inhibits said activity; (e) contacting an isolated feline CD40 protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has CD40 ligand binding activity; and determining if said putative inhibitory compound inhibits said activity; (f) contacting an isolated canine CD154 protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has B cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity; (g) contacting an isolated feline CD154 protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has B cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity; (h) contacting an isolated canine IL-5 protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has TF-1 cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity; (i) contacting an isolated canine IL-13 protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has TF-1 cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity; (j) contacting an isolated feline IFN $\alpha$  protein of the present invention with a putative inhibitory compound under conditions in which, in the absence

of said compound, said protein has inhibition of proliferation of GM-CSF stimulated TF-1 cell activity; and determining if said putative inhibitory compound inhibits said activity; or (k) contacting an isolated feline GMCSF protein of the present invention with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has TF-1 cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity.

### DETAILED DESCRIPTION OF THE INVENTION

The present invention provides for isolated canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF proteins, isolated canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecules, antibodies directed against canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF proteins, and compounds derived therefrom that regulate the immune response of an animal (e.g. inhibitors, antibodies and peptides).

Canine IL-4 protein can refer to a canine IL-4 protein, including homologs thereof. Canine Flt-3 ligand protein can refer to a canine Flt-3 ligand, including homologs thereof, and feline Flt-3 ligand can refer to feline Flt-3 ligand, including homologs thereof. Canine CD40 can refer to a canine CD40, including homologs thereof; feline CD40 can refer to a feline CD40, including homologs thereof. Canine CD154 can refer to a canine CD154, including homologs thereof; feline CD154 can refer to a feline

CD154, including homologs thereof. Canine IL-5 can refer to canine IL-5, including homologs thereof; canine IL-13 can refer to canine IL-13, including homologs thereof. Feline IFN $\alpha$  can refer to a feline IFN $\alpha$ , including homologs thereof, and feline GM-CSF can refer to a feline GM-CSF, including homologs thereof. As used herein, the phrase

5 “regulate an immune response” refers to modulating the activity of cells or molecules involved in an immune response. The term “regulate” can refer to increasing or decreasing an immune response. Regulation of an immune response can be determined using methods known in the art as well as methods disclosed herein. The term, “immunoregulatory protein” refers to a protein that can modulate the activity of cells or

10 of molecules involved in an immune response. An immunoregulatory protein of the present invention refers to a canine IL-4, a canine and/or feline CD40, a canine and/or feline Flt3 ligand, a canine and/or feline CD154, a canine IL-5, a canine IL-13, a feline IFN $\alpha$ , and/or a feline GM-CSF protein as described herein. As used herein, the terms isolated canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine

15 or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF proteins and/or isolated canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecules refer to canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline

20 CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF proteins and/or canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecules derived from mammals and,

as such, can be obtained from their natural source, or can be produced using, for example, recombinant nucleic acid technology or chemical synthesis. Also included in the present invention is the use of these proteins, nucleic acid molecules, antibodies, and/or compounds derived therefrom as therapeutic compositions to regulate the immune  
 5 response of an animal as well as in other applications, such as those disclosed below.

One embodiment of the present invention is an isolated protein that includes a canine IL-4 protein, a canine and/or feline Flt-3 ligand protein, a canine and/or feline CD40 protein, a canine and/or feline CD154 protein, a canine interleukin-5 protein, a canine interleukin-13 protein, a feline interferon alpha protein, and/or a feline GM-CSF  
 10 protein. It is to be noted that the term “a” or “an” entity refers to one or more of that entity; for example, a protein refers to one or more proteins or at least one protein. As such, the terms “a” (or “an”), “one or more” and “at least one” can be used interchangeably herein. It is also to be noted that the terms “comprising”, “including”, and “having” can be used interchangeably. According to the present invention, an  
 15 isolated, or biologically pure, protein, is a protein that has been removed from its natural milieu. As such, “isolated” and/or “biologically pure” do not necessarily reflect the extent to which the protein has been purified. An isolated protein of the present invention can be obtained from its natural source, can be produced using recombinant DNA technology, or can be produced by chemical synthesis. Nucleic acid molecules of the  
 20 present invention of known length isolated from *Canis familiaris* are denoted as follows:

IL-4 is denoted as nCaIL-4<sub>x</sub>, for example, nCaIL-4<sub>549</sub>, wherein “#” refers to the number of nucleotides in that molecule; and in a similar fashion, Flt-3 ligand nucleic acid molecules are referred to as nCaFlt3L<sub>x</sub>; CD40, nCaCD40<sub>x</sub>; CD154, nCaCD154<sub>x</sub>; IL-5, nCaIL-5<sub>x</sub>; and

IL-13, nCaIL-13<sub>x</sub>. In a similar fashion, Flt-3 ligand nucleic acid molecules of the present invention of known length isolated from *Felis catus* are denoted as nFeFlt3L<sub>x</sub>, CD40, nFeCD40<sub>x</sub>; CD154, nFeCD154<sub>x</sub>; IFN $\alpha$ , nFeIFN $\alpha$ <sub>x</sub>; and GM-CSF (also denoted GMCSF), nFeGM-CSF<sub>x</sub>. Similarly, proteins of the present invention of known length isolated

5 from *Felis catus* are denoted as PFeFlt3l<sub>x</sub>, PFeCD40<sub>x</sub>, PFeCD154<sub>x</sub>, PFeIFN $\alpha$ <sub>x</sub>, and/or PFeGM-CSF<sub>x</sub>; and proteins of the present invention of known length isolated from *Canis familiaris* are denoted PCaIL-4<sub>x</sub>, PCaFlt3L<sub>x</sub>, PCaCD40<sub>x</sub>, PCaCD154<sub>x</sub>, PCaIL-5<sub>x</sub>, and/or PCaIL-13<sub>x</sub>.

As used herein, an isolated canine interleukin-4, canine or feline Flt-3 ligand,

10 canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, and/or feline GM-CSF ligand protein of the present invention (i.e., an canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, respectively) can be a full-length protein or any homolog of such

15 a protein. An isolated IL-4 protein of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's ability to elicit an immune response against, (or to) an IL-4 protein, bind to an IL-4 receptor, stimulate B cell differentiation or activation or stimulate production of immunoglobulin by a B cell. An isolated Flt-3 ligand protein of the present invention, including a homolog, can be

20 identified in a straight-forward manner by the protein's ability to elicit an immune response against a Flt-3 ligand protein, bind to Flt-3 receptor or stimulate Flt-3 receptor-bearing hematopoietic stem cells, early hematopoietic progenitor cells or immature lymphocytes. An isolated CD40 protein of the present invention, including a homolog,

can be identified in a straight-forward manner by the protein's ability to elicit an immune response against a CD40 protein, bind to CD154 or stimulate CD154-bearing B cells, T cells, and/or epithelial cells. An isolated CD154 protein of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's

5 ability to elicit an immune response to a CD154 protein, bind to CD40 or stimulate CD40-bearing B cells, T cells, and/or epithelial cells. An isolated IL-5 protein of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's ability to elicit an immune response to an IL-5 protein, bind to an IL-5 receptor, and/or stimulate eosinophils and/or cause thymocytes to produce cytotoxic T

10 cells. An isolated IL-13 protein of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's ability to elicit an immune response to an IL-13 protein, bind to an IL-13 receptor, and/or stimulate B cells, up-regulate expression of MHC class II and/or CD23 on monocytes, macrophages and/or B cells; and/or inhibition of proinflammatory cytokines. An isolated interferon alpha

15 protein of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's ability to elicit an immune response to an interferon alpha protein, bind to an interferon alpha receptor, and/or activate NK cells and/or inhibit viral replication. An isolated GM-CSF protein of the present invention, including a homolog, can be identified in a straight-forward manner by the protein's ability to elicit

20 an immune response to a GM-CSF protein, bind to a GM-CSF receptor, and/or activate granulocytes and/or macrophages. Examples of protein homologs of the present invention include immunoregulatory proteins of the present invention in which amino acids have been deleted (e.g., a truncated version of the protein, such as a peptide),



inserted, inverted, substituted and/or derivatized (e.g., by glycosylation, phosphorylation, acetylation, myristoylation, prenylation, palmitoylation, amidation and/or addition of glycerophosphatidyl inositol) such that the protein homolog includes at least one epitope capable of eliciting an immune response against the parent protein, of binding to an

5 antibody directed against the parent protein and/or of binding to the parent's receptor, where the term parent refers to the longer and/or full-length protein that the homolog is derived from. That is, when the homolog is administered to an animal as an immunogen, using techniques known to those skilled in the art, the animal will produce an immune response against at least one epitope of an immunoregulatory protein of the present

10 invention, depending upon which protein is administered to an animal. The ability of a protein to effect an immune response can be measured using techniques known to those skilled in the art. As used herein, the term "epitope" refers to the smallest portion of a protein capable of selectively binding to the antigen binding site of an antibody. It is well accepted by those skilled in the art that the minimal size of a protein epitope capable of

15 selectively binding to the antigen binding site of an antibody is about five or six to seven amino acids.

Homologs of immunoregulatory proteins of the present invention can be the result of natural allelic variation, including natural mutation. Protein homologs of the present invention can also be produced using techniques known in the art including, but not

20 limited to, direct modifications to the protein and/or modifications to the gene encoding the protein using, for example, classic or recombinant DNA techniques to effect random or targeted mutagenesis.

Immunoregulatory proteins of the present invention include variants of a full-length protein of a protein of the present invention. Such variants include proteins that are less than full-length. As used herein, variants of the present invention refer to nucleic acid molecules that are naturally-occurring as defined below, and may result from alternative RNA splicing, alternative termination of an amino acid sequence or DNA recombination. Examples of variants include allelic variants as defined below. It is to be noted that a variant is an example of a homolog of the present invention.

Immunoregulatory proteins of the present invention are encoded by nucleic acid molecules of the present invention. As used herein, an IL-4 nucleic acid molecule includes nucleic acid sequences related to a natural canine IL-4 gene. As used herein, a Flt-3 ligand nucleic acid molecule includes nucleic acid sequences related to a natural canine Flt-3 ligand gene. As used herein, a CD40 nucleic acid molecule includes nucleic acid sequences related to a natural CD40 gene. As used herein, a CD154 nucleic acid molecule includes nucleic acid sequences related to a natural CD154 gene. As used herein, an IL-5 nucleic acid molecule includes nucleic acid sequences related to a natural IL-5 gene. As used herein, an IL-13 nucleic acid molecule includes nucleic acid sequences related to a natural IL-13 gene. As used herein, an IFN $\alpha$  nucleic acid molecule includes nucleic acid sequences related to a natural IFN $\alpha$  gene. As used herein, a GM-CSF nucleic acid molecule includes nucleic acid sequences related to a natural GM-CSF gene. As used herein, a canine IL-4, a canine and/or feline CD40, a canine and/or feline Flt3 ligand, a canine and/or feline CD154, a canine IL-5, a canine IL-13, a feline IFN $\alpha$ , and/or a feline GM-CSF gene refers to the natural genomic elements that encode an canine IL-4, a canine and/or feline CD40, a canine and/or feline Flt3 ligand, a canine

and/or feline CD154, a canine IL-5, a canine IL-13, a feline IFN $\alpha$ , and/or a feline GM-CSF protein, respectively, and includes all regions such as regulatory regions that control production of the protein encoded by the gene (such as, but not limited to, transcription, translation or post-translation control regions) as well as the coding region itself, and any

5 introns or non-translated coding regions. As used herein, a gene that “includes” or “comprises” a sequence may include that sequence in one contiguous array, or may include the sequence as fragmented exons. As used herein, the term “coding region” refers to a continuous linear array of nucleotides that translates into a protein. A full-length coding region is that region that is translated into a full-length, i.e., a complete,

10 protein as would be initially translated in its natural milieu, prior to any post-translational modifications.

In one embodiment, an IL-4 gene of the present invention includes the nucleic acid sequence SEQ ID NO:1, as well as the complement of SEQ ID NO:1. Nucleic acid sequence SEQ ID NO:1 represents the deduced sequence of the coding strand of a cDNA

15 (complementary DNA) denoted herein as nucleic acid molecule nCaIL-4<sub>549</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nCaIL-4<sub>549</sub> comprises an apparently full-length coding region of canine IL-4. The complement of SEQ ID NO:1 (represented herein by SEQ ID NO:3) refers to the nucleic acid sequence of the strand fully complementary to the strand having SEQ ID NO:1, which can easily be

20 determined by those skilled in the art. Likewise, a nucleic acid sequence complement of any nucleic acid sequence of the present invention refers to the nucleic acid sequence of the nucleic acid strand that is fully complementary to (i.e., can form a double helix with) the strand for which the sequence is cited. It should be noted that since nucleic acid

sequencing technology is not entirely error-free, SEQ ID NO:1 (as well as other nucleic acid and protein sequences presented herein) represents an apparent nucleic acid sequence of the nucleic acid molecule encoding an immunoregulatory protein of the present invention.

5           In another embodiment, a Flt-3 ligand gene of the present invention includes the nucleic acid sequence SEQ ID NO:6, as well as the complement represented by SEQ ID NO:8. Nucleic acid sequence SEQ ID NO:6 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nCaFlt3L<sub>1013</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nCaFlt3L<sub>1013</sub>  
10       comprises an apparently full-length coding region of canine Flt-3 ligand.

          In another embodiment, a Flt-3 ligand gene of the present invention includes the nucleic acid sequence SEQ ID NO:43, as well as the complement represented by SEQ ID NO:45. Nucleic acid sequence SEQ ID NO:43 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nFeFlt3L<sub>942</sub>, the  
15       production of which is disclosed in the Examples. Nucleic acid molecule nFeFlt3L<sub>942</sub> comprises an apparently full-length coding region of feline Flt-3 ligand.

          In another embodiment, a CD40 gene of the present invention includes the nucleic acid sequence SEQ ID NO:52, as well as the complement represented by SEQ ID NO:54. Nucleic acid sequence SEQ ID NO:52 represents the deduced sequence of the coding  
20       strand of a cDNA denoted herein as nucleic acid molecule nCaCD40<sub>1425</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nCaCD40<sub>1425</sub> comprises an apparently full-length coding region of canine CD40.

In another embodiment, a CD40 gene of the present invention includes the nucleic acid sequence SEQ ID NO:60, as well as the complement represented by SEQ ID NO:62. Nucleic acid sequence SEQ ID NO:60 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nFeCD40<sub>336</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nFeCD40<sub>336</sub> comprises an apparent portion of the coding region of feline CD40.

In another embodiment, a CD154 gene of the present invention includes the nucleic acid sequence SEQ ID NO:64, as well as the complement represented by SEQ ID NO:66. Nucleic acid sequence SEQ ID NO:64 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nCaCD154<sub>1878</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nCaCD154<sub>1878</sub> comprises an apparently full-length coding region of canine CD154.

In another embodiment, a CD154 gene of the present invention includes the nucleic acid sequence SEQ ID NO:72, as well as the complement represented by SEQ ID NO:74. Nucleic acid sequence SEQ ID NO:72 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nFeCD154<sub>885</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nFeCD154<sub>885</sub> comprises an apparently full-length coding region of feline CD154.

In another embodiment, an IL-5 gene of the present invention includes the nucleic acid sequence SEQ ID NO:80, as well as the complement represented by SEQ ID NO:82. Nucleic acid sequence SEQ ID NO:80 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nCaIL-5<sub>610</sub>, the production of

which is disclosed in the Examples. Nucleic acid molecule nCaIL-5<sub>610</sub> comprises an apparently full-length coding region of canine IL-5.

In another embodiment, an IL-13 gene of the present invention includes the nucleic acid sequence SEQ ID NO:91, as well as the complement represented by SEQ ID NO:93. Nucleic acid sequence SEQ ID NO:91 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nCaIL-13<sub>1302</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nCaIL-13<sub>1302</sub> comprises an apparently full-length coding region of canine IL-13.

In another embodiment, an IFN $\alpha$  gene of the present invention includes the nucleic acid sequence SEQ ID NO:107, SEQ ID NO:110, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:161, SEQ ID NO:164, SEQ ID NO:167, or SEQ ID NO:170, as well as the complement represented by, respectively, SEQ ID NO:109, SEQ ID NO:112, SEQ ID NO:157, SEQ ID NO:160, SEQ ID NO:163, or SEQ ID NO:166, SEQ ID NO:169, and SEQ ID NO:172. Nucleic acid sequences SEQ ID NO:107, SEQ ID NO:110, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:161, SEQ ID NO:164, SEQ ID NO:167, and SEQ ID NO:170 represent the deduced sequences of the coding strands of cDNAs denoted herein as nucleic acid molecules nFeIFN $\alpha$ <sub>567a</sub>, nFeIFN $\alpha$ <sub>567b</sub>, nFeIFN $\alpha$ <sub>567c</sub>, nFeIFN $\alpha$ <sub>498c</sub>, nFeIFN $\alpha$ <sub>582d</sub>, nFeIFN $\alpha$ <sub>513d</sub>, nFeIFN $\alpha$ <sub>567e</sub>, and nFeIFN $\alpha$ <sub>498e</sub>, respectively. Each of these nucleic acid molecules, the production of which is disclosed in the Examples, comprises an apparently full-length coding region of a feline IFN $\alpha$  protein.

In another embodiment, a GM-CSF gene of the present invention includes the nucleic acid sequence SEQ ID NO:119, as well as the complement represented by SEQ



ID NO:121. Nucleic acid sequence SEQ ID NO:119 represents the deduced sequence of the coding strand of a cDNA denoted herein as nucleic acid molecule nFeGM-CSF<sub>444</sub>, the production of which is disclosed in the Examples. Nucleic acid molecule nFeGM-CSF<sub>444</sub> comprises an apparently full-length coding region of feline GM-CSF.

5 Additional immunoregulatory nucleic acid molecules and proteins of the present invention having specific sequence identifiers are described in Table 1.

Table 1. Sequence identification numbers (SEQ ID NOs) and their corresponding nucleic acid molecules or proteins.

SEQ ID NO:	DESCRIPTION
1	nCaIL-4 <sub>549</sub> coding strand
2	PCaIL-4 <sub>132</sub>
3	nCaIL-4 <sub>549</sub> complementary strand
4	nCaIL-4 <sub>396</sub> coding strand
5	nCaIL-4 <sub>396</sub> complementary strand
6	nCaFlt3L <sub>1013</sub> coding strand
7	PCaFlt3L <sub>294</sub>
8	nCaFlt3L <sub>1013</sub> complementary strand
9	nCaFlt3L <sub>882</sub> coding strand
10	nCaFlt3L <sub>882</sub> complementary strand
19	nCaIL-4 <sub>324</sub> coding strand
20	PCaIL-4 <sub>108</sub>
21	nCaIL-4 <sub>324</sub> complementary strand
22	nCaFlt3L <sub>804</sub> coding strand
23	PCaFlt3L <sub>268</sub>
24	nCaFlt3L <sub>804</sub> complementary strand
25	nCaFlt3L <sub>985</sub> coding strand

SEQ ID NO:	DESCRIPTION
26	PCaFlt3L <sub>276</sub>
27	nCaFlt3L <sub>985</sub> complementary strand
28	nCaFlt3L <sub>828</sub> coding strand
29	nCaFlt3L <sub>828</sub> complementary strand
30	nCaFlt3L <sub>750</sub> coding strand
31	PCaFlt3L <sub>250</sub>
32	nCaFlt3L <sub>750</sub> complementary strand
33	nCaFlt3L <sub>1019</sub> coding strand
34	PCaFlt3L <sub>31</sub>
35	nCaFlt3L <sub>1019</sub> complementary strand
36	nCaFlt3L <sub>93</sub> coding strand
37	nCaFlt3L <sub>93</sub> complementary strand
41	nFeFlt3L <sub>395</sub> coding strand
42	nFeFlt3L <sub>793</sub> coding strand
43	nFeFlt3L <sub>942</sub> coding strand
44	PFeFlt3L <sub>291</sub>
45	nFeFlt3L <sub>942</sub> complementary strand
46	nFeFlt3L <sub>873</sub> coding strand
47	nFeFlt3L <sub>873</sub> complementary strand
48	nFeFlt3L <sub>795</sub> coding strand
49	PFeFlt3L <sub>265</sub>
50	nFeFlt3L <sub>795</sub> complementary strand
51	nCaCD40 <sub>321</sub> coding strand
52	nCaCD40 <sub>1425</sub> coding strand
53	PCaCD40 <sub>274</sub>
54	nCaCD40 <sub>1425</sub> complementary strand

SEQ ID NO:	DESCRIPTION
55	nCaCD40 <sub>822</sub> coding strand
56	nCaCD40 <sub>822</sub> complementary strand
57	nCaCD40 <sub>765</sub> coding strand
58	PCaCD40 <sub>255</sub>
59	nCaCD40 <sub>765</sub> complementary strand
60	nFeCD40 <sub>336</sub> coding strand
61	PFeCD40 <sub>112</sub>
62	nFeCD40 <sub>336</sub> complementary strand
63	nCaCD154 <sub>390</sub> coding strand
64	nCaCD154 <sub>1878</sub> coding strand
65	PCaCD154 <sub>260</sub>
66	nCaCD154 <sub>1878</sub> complementary strand
67	nCaCD154 <sub>780</sub> coding strand
68	nCaCD154 <sub>780</sub> complementary strand
69	nCaCD154 <sub>633</sub> coding strand
70	PCaCD154 <sub>211</sub>
71	nCaCD154 <sub>633</sub> complementary strand
72	nFeCD154 <sub>885</sub> coding strand
73	PFeCD154 <sub>260</sub>
74	nFeCD154 <sub>885</sub> complementary strand
75	nFeCD154 <sub>780</sub> coding strand
76	nFeCD154 <sub>780</sub> complementary strand
77	nFeCD154 <sub>633</sub> coding strand
78	PFeCD154 <sub>211</sub>
79	nFeCD154 <sub>633</sub> complementary strand
80	nCaIL-5 <sub>610</sub> coding strand

SEQ ID NO:	DESCRIPTION
81	PCaIL-5 <sub>134</sub>
82	nCaIL-5 <sub>610</sub> complementary strand
83	nCaIL-5 <sub>402</sub> coding strand
84	nIL-5 <sub>402</sub> complementary strand
5 85	nCaIL-5 <sub>345</sub> coding strand
86	PCaIL-5 <sub>115</sub>
87	nCaIL-5 <sub>345</sub> complementary strand
88	nCaIL-13 <sub>166</sub> coding strand
89	nCaIL-13 <sub>272</sub> coding strand
10 90	nCaIL-13 <sub>278</sub> coding strand
91	nCaIL-13 <sub>1302</sub> coding strand
92	PCaIL-13 <sub>131</sub>
93	nCaIL-13 <sub>1302</sub> complementary strand
94	nCaIL-13 <sub>393</sub> coding strand
15 95	nCaIL-13 <sub>393</sub> complementary strand
96	nCaIL-13 <sub>333</sub> coding strand
97	PaIL-13 <sub>111</sub>
98	nCaIL-13 <sub>333</sub> complementary strand
99	nCaIL-13 <sub>1269</sub> coding strand
20 100	PCaIL-13 <sub>130</sub>
101	nCaIL-13 <sub>1269</sub> complementary strand
102	nCaIL-13 <sub>390</sub> coding strand
103	nCaIL-13 <sub>390</sub> complementary strand
104	nCaIL-13 <sub>330</sub> coding strand
25 105	PCaIL-13 <sub>110</sub>
106	nCaIL-13 <sub>330</sub> complementary strand

SEQ ID NO:	DESCRIPTION
107	nFeIFN $\alpha_{567a}$ coding strand
108	PFeIFN $\alpha_{189a}$
109	nFeIFN $\alpha_{567a}$ complementary strand
110	nFeIFN $\alpha_{567b}$ coding strand
111	PFeIFN $\alpha_{189b}$
112	nFeIFN $\alpha_{567b}$ complementary strand
113	nFeIFN $\alpha_{498a}$ coding strand
114	PFeIFN $\alpha_{166a}$
115	nFeIFN $\alpha_{498a}$ complementary strand
116	nFeFeIFN $\alpha_{498b}$ coding strand
117	PFeIFN $\alpha_{166b}$
118	nFeIFN $\alpha_{498b}$ complementary strand
119	nFeGMCSF $_{444}$ coding strand
120	PFeGMCSF $_{144}$
121	nFeGMCSF $_{444}$ complementary strand
122	nFeGMCSF $_{432}$ coding strand
123	nFeGMCSF $_{432}$ complementary strand
124	nFeGMCSF $_{381}$ coding strand
125	PFeGMCSF $_{127}$
126	nFeGMCSF $_{381}$ complementary strand
155	nFeIFN $\alpha_{567c}$
156	PFeIFN $\alpha_{189c}$
157	nFeIFN $\alpha_{567c}$ complementary strand
158	nFeIFN $\alpha_{498c}$
159	PFeIFN $\alpha_{166c}$
160	nFeIFN $\alpha_{498c}$ complementary strand

SEQ ID NO:	DESCRIPTION
161	nFeIFN $\alpha_{582d}$
162	PFeIFN $\alpha_{194d}$
163	nFeIFN $\alpha_{582d}$ complementary strand
164	nFeIFN $\alpha_{513d}$
165	PFeIFN $\alpha_{171d}$
166	nFeIFN $\alpha_{513d}$ complementary strand
167	nFeIFN $\alpha_{567e}$
168	PFeIFN $\alpha_{189e}$
169	nFeIFN $\alpha_{567e}$ complementary strand
170	nFeIFN $\alpha_{498e}$
171	PFeIFN $\alpha_{166e}$
172	nFeIFN $\alpha_{498e}$ complementary strand

In another embodiment, an IL-4 gene or nucleic acid molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, SEQ ID NO:21, and/or any other IL-4 nucleic acid sequence cited herein. In another embodiment, a Flt-3 ligand gene or nucleic acid molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50 and/or any other Flt-3 ligand nucleic acid sequence cited herein. In another embodiment, a CD40 gene or nucleic acid



molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62 and/or any other CD40 nucleic acid sequence cited herein. In another embodiment, a CD154 gene or nucleic acid

5 molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79 and/or any other CD154 nucleic acid sequence cited herein. In another embodiment, an IL-5 gene or nucleic acid molecule can be an

10 allelic variant that includes a similar but not identical sequence to SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:87 and/or any other IL-5 nucleic acid sequence cited herein. In another embodiment, an IL-13 gene or nucleic acid molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID

15 NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:106 and/or any other IL-13 nucleic acid sequence cited herein. In another embodiment, an IFN $\alpha$  gene or nucleic acid molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:107, SEQ ID NO:109, SEQ

20 ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170 and/or SEQ ID NO:172, and/or any other IFN $\alpha$  nucleic acid

sequence cited herein. In another embodiment, a GM-CSF gene or nucleic acid molecule can be an allelic variant that includes a similar but not identical sequence to SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, and/or SEQ ID NO:126 and/or any other GM-CSF nucleic acid cited herein. An allelic variant

5 of a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF gene, including the particular SEQ ID NO's cited herein, is a gene that occurs at essentially the same locus (or loci) in the genome as the gene including the particular SEQ ID NO's cited herein, but which, due to natural variations caused by, for

10 example, mutation or recombination, has a similar but not identical sequence. Also included in the term allelic variant are allelic variants of cDNAs derived from such genes. Because natural selection typically selects against alterations that affect function, allelic variants usually encode proteins having similar activity to that of the protein encoded by the gene to which they are being compared. Allelic variants of genes or nucleic acid

15 molecules can also comprise alterations in the 5' or 3' untranslated regions of the gene (e.g., in regulatory control regions), or can involve alternative splicing of a nascent transcript, thereby bringing alternative exons into juxtaposition. Allelic variants are well known to those skilled in the art and would be expected to be found within a given animal, since the respective genomes are diploid, and sexual reproduction will result in

20 the reassortment of alleles.

The minimal size of an canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein homolog of the present invention is a

size sufficient to be encoded by a nucleic acid molecule capable of forming a stable hybrid (i.e., hybridize under stringent hybridization conditions) with the complementary sequence of a nucleic acid molecule encoding the corresponding natural protein.

Stringent hybridization conditions are determined based on defined physical properties of the gene to which the nucleic acid molecule is being hybridized, and can be defined mathematically. Stringent hybridization conditions are those experimental parameters that allow an individual skilled in the art to identify significant similarities between heterologous nucleic acid molecules. These conditions are well known to those skilled in the art. See, for example, Sambrook, *et al.*, 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Labs Press, and Meinkoth, *et al.*, 1984, *Anal. Biochem.* 138, 267-284, each of which is incorporated herein by this reference. As explained in detail in the cited references, the determination of hybridization conditions involves the manipulation of a set of variables including the ionic strength (M, in moles/liter), the hybridization temperature (°C), the concentration of nucleic acid helix destabilizing agents, such as formamide, the average length of the shortest hybrid duplex (n), and the percent G + C composition of the fragment to which an unknown nucleic acid molecule is being hybridized. For nucleic acid molecules of at least about 150 nucleotides, these variables are inserted into a standard mathematical formula to calculate the melting temperature, or  $T_m$ , of a given nucleic acid molecule. As defined in the formula below,  $T_m$  is the temperature at which two complementary nucleic acid molecule strands will disassociate, assuming 100% complementarity between the two strands:

$$T_m = 81.5^{\circ}\text{C} + 16.6 \log M + 0.41(\%G + C) - 500/n - 0.61(\%\text{formamide}).$$

For nucleic acid molecules smaller than about 50 nucleotides, hybrid stability is defined by the dissociation temperature ( $T_d$ ), which is defined as the temperature at which 50% of the duplexes dissociate. For these smaller molecules, the stability at a standard ionic strength is defined by the following equation:

$$T_d = 4(G + C) + 2(A + T).$$

A temperature of 5°C below  $T_d$  is used to detect hybridization between perfectly matched molecules.

Also well known to those skilled in the art is how base pair mismatch, i.e. differences between two nucleic acid molecules being compared, including non-complementarity of bases at a given location, and gaps due to insertion or deletion of one or more bases at a given location on either of the nucleic acid molecules being compared, will affect  $T_m$  or  $T_d$  for nucleic acid molecules of different sizes. For example,  $T_m$  decreases about 1°C for each 1% of mismatched base pairs for hybrids greater than about 150 bp, and  $T_d$  decreases about 5°C for each mismatched base pair for hybrids below about 50 bp. Conditions for hybrids between about 50 and about 150 base pairs can be determined empirically and without undue experimentation using standard laboratory procedures well known to those skilled in the art. These simple procedures allow one skilled in the art to set the hybridization conditions, by altering, for example, the salt concentration, the formamide concentration or the temperature, so that only nucleic acid hybrids with greater than a specified % base pair mismatch will hybridize. Stringent hybridization conditions are commonly understood by those skilled in the art to be those experimental conditions that will allow about 30% base pair mismatch, i.e., about 70% identity. Because one skilled in the art can easily determine whether a given nucleic acid

molecule to be tested is less than or greater than about 50 nucleotides, and can therefore choose the appropriate formula for determining hybridization conditions, he or she can determine whether the nucleic acid molecule will hybridize with a given gene or specified nucleic acid molecule under stringent hybridization conditions and similarly whether the

5 nucleic acid molecule will hybridize under conditions designed to allow a desired amount of base pair mismatch.

Hybridization reactions are often carried out by attaching the nucleic acid molecule to be hybridized to a solid support such as a membrane, and then hybridizing with a labeled nucleic acid molecule, typically referred to as a probe, suspended in a

10 hybridization solution. Examples of common hybridization reaction techniques include, but are not limited to, the well-known Southern and northern blotting procedures. Typically, the actual hybridization reaction is done under non-stringent conditions, i.e., at a lower temperature and/or a higher salt concentration, and then high stringency is achieved by washing the membrane in a solution with a higher temperature and/or lower

15 salt concentration in order to achieve the desired stringency.

Preferred portions, or fragments, of a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF, protein of the present invention include at least 15 amino acids, at least 20 amino acids, at least 25 amino acids, at least

20 30 amino acids, at least 35 amino acids, at least 40 amino acids, at least 45 amino acids, at least 50 amino acids, at least 60 amino acids, at least 75 amino acids or at least 100 amino acids. An IL-4, IL-5, and/or IL-13 protein of the present invention can include at least a portion of an IL-4, IL-5, and/or IL-13 protein that is capable of binding to an IL-4,

IL-5, and/or IL-13 receptor, respectively. IL-4, IL-5, and IL-13 receptors are known to those of skill in the art, and are described in Janeway et al., in *Immunobiology, the Immune System in Health and Disease*, Garland Publishing, Inc., NY, 1996 (which is incorporated herein by this reference in its entirety). The IL-4, IL-5, and/or IL-13

5 receptor-binding portion of an IL-4, IL-5, and/or IL-13 protein, respectively, can be determined by incubating the protein with an isolated IL-4, IL-5, and/or IL-13 receptor, as appropriate, or a cell having an IL-4, IL-5, and/or IL-13 receptor on its surface, as appropriate. IL-4, IL-5, and/or IL-13 protein binding to purified IL-4, IL-5, and/or IL-13 receptor, respectively, can be determined using methods known in the art including

10 Biacore® screening, confocal immunofluorescent microscopy, immunoprecipitation, gel chromatography, determination of inhibition of binding of antibodies that bind specifically to the IL-4, IL-5, and/or IL-13 binding domain of an IL-4, IL-5, and/or IL-13 receptor, ELISA using an IL-4, IL-5, and/or IL-13 receptor, respectively, labeled with a detectable tag such as an enzyme or chemiluminescent tag or yeast-2 hybrid technology.

15 A Flt-3 ligand protein of the present invention can include at least a portion of a Flt-3 ligand protein that is capable of binding to Flt-3 receptor or stimulating Flt-3 receptor-bearing hematopoietic stem cells, early hematopoietic progenitor cells or immature lymphocytes. Flt-3 receptors are known to those of skill in the art, and are described in Drexler, *Leukemia*, vol. 10, pp. 588-599, 1996 (which is incorporated herein in its

20 entirety by this reference). The Flt-3 receptor-binding portion of a Flt-3 ligand protein can be determined by incubating the protein with isolated Flt-3 receptor or a cell having a Flt-3 receptor on its surface. Flt-3 ligand protein binding to purified Flt-3 receptor can be determined using methods known in the art including Biacore® screening, confocal



immunofluorescent microscopy, immunoprecipitation, gel chromatography, determination of inhibition of binding of antibodies that bind specifically to the Flt-3 ligand binding domain of a Flt-3 receptor, ELISA using a Flt-3 receptor labeled with a detectable tag such as an enzyme or chemiluminescent tag or yeast-2 hybrid technology.

- 5 A CD40 and/or CD154 protein of the present invention can include at least a portion of a CD40 and/or CD154 protein that is capable of binding to a CD40 and/or CD154 receptor, respectively, or stimulating CD40 and/or CD154 receptor-bearing hematopoietic stem cells, early hematopoietic progenitor cells or immature lymphocytes. The CD40 and/or CD154 receptor-binding portion of a CD40 and/or CD154 protein can be determined by
- 10 incubating the protein with isolated CD40 and/or CD154 receptor, as appropriate, or a cell having a CD40 and/or CD154 receptor on its surface, as appropriate. CD40 and/or CD154 protein binding to CD154 and/or CD40, respectively, can be determined using methods known in the art including Biacore® screening, confocal immunofluorescent microscopy, immunoprecipitation, gel chromatography, determination of inhibition of
- 15 binding of antibodies that bind specifically to the CD40 and/or CD154 binding domain of CD40 and/or CD154, as appropriate, ELISA using a CD40 and/or CD154 labeled with a detectable tag such as an enzyme or chemiluminescent tag or yeast-2 hybrid technology.

- The present invention also includes mimetopes of canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5,
- 20 canine interleukin-13, feline interferon alpha, or feline GM-CSF proteins of the present invention. As used herein, a mimetope of an immunoregulatory protein of the present invention refers to any compound that is able to mimic the activity of such a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline

CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, respectively, often because the mimetope has a structure that mimics the particular protein. Mimetopes can be, but are not limited to: peptides that have been modified to decrease their susceptibility to degradation such as all-D retro peptides;

5 anti-idiotypic and/or catalytic antibodies, or fragments thereof; non-proteinaceous immunogenic portions of an isolated protein (e.g., carbohydrate structures); and/or synthetic or natural organic molecules, including nucleic acids. Such mimetopes can be designed using computer-generated structures of proteins of the present invention.

Mimetopes can also be obtained by generating random samples of molecules, such as

10 oligonucleotides, peptides or other organic molecules, and screening such samples by affinity chromatography techniques using the corresponding binding partner.

One embodiment of an immunoregulatory protein of the present invention is a fusion protein that includes either a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-

15 13, feline interferon alpha, or feline GM-CSF protein-containing domain, each attached to one or more fusion segments. Suitable fusion segments for use with the present invention include, but are not limited to, segments that can: link two or more immunoregulatory proteins of the present invention, to form multimeric forms of an immunoregulatory protein of the present invention; enhance a protein's stability; act as an immunopotentiator

20 to enhance an immune response against an canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein; and/or assist in purification of an canine interleukin-4, canine or feline Flt-3 ligand, canine or feline

CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein (e.g., by affinity chromatography). A suitable fusion segment can be a domain of any size that has the desired function (e.g., imparts increased stability, imparts increased immunogenicity to a protein, and/or simplifies purification of a protein). Fusion segments can be joined to amino and/or carboxyl termini of the IL-4-containing domain, or the Flt-3 ligand-containing domain, or the CD40-containing domain, or the CD154-containing domain, or the IL-5-containing domain, or the IL-13-containing domain, or the IFN $\alpha$ -containing domain, or GM-CSF-containing domain, of a protein and can be susceptible to cleavage in order to enable straight-forward recovery of either canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, respectively. Fusion proteins are preferably produced by culturing a recombinant cell transformed with a fusion nucleic acid molecule that encodes a protein including the fusion segment attached to either the carboxyl and/or amino terminal end of an canine interleukin-4-, canine or feline Flt-3 ligand-, canine or feline CD40-, canine or feline CD154-, canine interleukin-5-, canine interleukin-13-, feline interferon alpha-, or feline GM-CSF-containing domain. Preferred fusion segments include a metal binding domain (e.g., a poly-histidine segment); an immunoglobulin binding domain (e.g., Protein A; Protein G; T cell; B cell; Fc receptor or complement protein antibody-binding domains); a sugar binding domain (e.g., a maltose binding domain); and/or a "tag" domain (e.g., at least a portion of -galactosidase, a strep tag peptide, a T7 tag peptide, a Flag<sup>TM</sup> peptide, or other domains that can be purified using compounds that bind to the domain, such as monoclonal antibodies). More

preferred fusion segments include metal binding domains, such as a poly-histidine segment; a maltose binding domain; a strep tag peptide, such as that available from Biometra in Tampa, FL; and an S10 peptide.

A suitable fusion segment that links one IL-4 protein to another IL-4 protein, or one Flt-3 ligand protein to another Flt-3 ligand protein, or one CD40 protein to another CD40 protein, or one CD154 protein to another CD154 protein, or one IL-5 protein to another IL-5 protein to another IL-5 protein, or one IL-13 protein to another IL-13 protein, or one IFN $\alpha$  protein to another IFN $\alpha$  protein, or one GM-CSF protein to another GM-CSF protein, includes any amino acid sequence that enables such proteins to be linked while maintaining the biological function of either the canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF, proteins, respectively. Selection of a suitable linker is dependent upon how many proteins are to be linked to form one multimeric molecule and from where on either the canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF molecule the linker extends. Preferably, a linker fusion segment of the present invention comprises a peptide of from about 6 amino acid residues to about 40 residues, more preferably from about 6 residues to about 30 residues in length.

In another embodiment, an canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein of the present invention also includes at least one additional protein segment that is capable of targeting either canine

interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, respectively, to a desired cell or receptive molecule. Such a multivalent targeting protein can be produced by culturing a cell transformed with a nucleic acid molecule comprising two or more nucleic acid domains joined together in such a manner that the resulting nucleic acid molecule is expressed as a multivalent targeting protein containing a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein or portion thereof and/or at least one targeting compound capable of delivering the canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, respectively, to a desired site in an animal.

Examples of multivalent targeting proteins include, but are not limited to, a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein of the present invention attached to one or more compounds that can bind to a receptive molecule on the surface of a cell located in an area of an animal where regulation of an immune response is desired. One of skill in the art can select appropriate targeting fusion segments depending upon the cell or receptive molecule being targeted.

Another example of a multivalent protein of the present invention includes, but is not limited to, a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon

alpha, or feline GM-CSF protein of the present invention attached to one or more proteins that are potentially antigenic in mammals. Thus, immunogenicity of the potentially antigenic protein could be enhanced by administering to a mammal together with an immunoregulatory protein of the present invention.

5 A naturally-occurring variant of a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein of the present invention is preferably isolated from (including isolation of the natural protein or production of the protein by recombinant or synthetic techniques) from mammals, including but not limited  
10 to dogs (i.e., canids), cats (i.e., felids), horses (i.e., equids), humans, cattle, chinchillas, ferrets, goats, mice, minks, rabbits, raccoons, rats, sheep, squirrels, swine, chickens, ostriches, quail and/or turkeys as well as other furry animals, pets, zoo animals, work animals and/or food animals. Particularly preferred animals from which to isolate canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline  
15 CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF proteins are dogs, cats, horses and/or humans.

A preferred isolated protein of the present invention is a protein encoded by at least one of the following nucleic acid molecules: nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, nCaIL-4<sub>324</sub>, nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>, nCaFlt3L<sub>985</sub>, nCaFlt3L<sub>1019</sub>,  
20 nCaFlt3L<sub>93</sub>, nCaFlt3L<sub>750</sub>, nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>, nFeFlt3L<sub>873</sub>, nFeFlt3L<sub>795</sub>, nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, nCaCD40<sub>765</sub>, nFeCD40<sub>336</sub>, nCaCD154<sub>390</sub>, nCaCD154<sub>1878</sub>, nCaCD154<sub>780</sub>, nCaCD154<sub>633</sub>, nFeCD154<sub>885</sub>, nFeCD154<sub>780</sub>, nFeCD154<sub>633</sub>, nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, nCaIL-5<sub>345</sub>, nCaIL-13<sub>166</sub>, nCaIL-13<sub>272</sub>, nCaIL-13<sub>278</sub>, nCaIL-13<sub>1302</sub>,



nCaIL-13<sub>393</sub>, nCaIL-13<sub>333</sub>, nCaIL-13<sub>1269</sub>, nCaIL-13<sub>390</sub>, nCaIL-13<sub>330</sub>, nFeIFN $\alpha$ <sub>567a</sub>,  
 nFeIFN $\alpha$ <sub>567b</sub>, nFeIFN $\alpha$ <sub>567c</sub>, nFeIFN $\alpha$ <sub>498a</sub>, nFeIFN $\alpha$ <sub>498b</sub>, nFeIFN $\alpha$ <sub>498c</sub>, nFeIFN $\alpha$ <sub>582d</sub>,  
 nFeIFN $\alpha$ <sub>513d</sub>, nFeIFN $\alpha$ <sub>567e</sub>, nFeIFN $\alpha$ <sub>498e</sub>, nFeGMCSF<sub>444</sub>, nFeGMCSF<sub>432</sub>, nFeGMCSF<sub>381</sub>

and/or allelic variants of any of these nucleic acid molecules. Also preferred is an

- 5 isolated protein that is encoded by a nucleic acid molecule the having nucleic acid  
 sequence SEQ ID NO:1, SEQ ID NO:4, SEQ ID NO:19, SEQ ID NO:6, SEQ ID NO:9,  
 SEQ ID NO:22, SEQ ID NO:25, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:33, SEQ  
 ID NO:36, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:46, SEQ ID  
 NO:48, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, SEQ ID NO:57, SEQ ID  
 10 NO:60, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, SEQ ID NO:69, SEQ ID  
 NO:72, SEQ ID NO:75, SEQ ID NO:77, SEQ ID NO:80, SEQ ID NO:83, SEQ ID  
 NO:85, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID  
 NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, SEQ ID NO:104, SEQ ID  
 NO:107, SEQ ID NO:110, SEQ ID NO:113, SEQ ID NO:116, SEQ ID NO:119, SEQ ID  
 15 NO:122, SEQ ID NO:124, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:161, SEQ ID  
 NO:164, SEQ ID NO:167, and SEQ ID NO:170; and/or an allelic variant of such a  
 nucleic acid molecule.

- Translation of SEQ ID NO:1, the coding strand of nCaIL-4<sub>549</sub>, yields a protein of  
 about 132 amino acids, denoted herein as PCaIL-4<sub>132</sub>, the amino acid sequence of which  
 20 is presented in SEQ ID NO:2, assuming an open reading frame having an initiation codon  
 spanning from nucleotide 43 through nucleotide 45 of SEQ ID NO:1 and a stop codon  
 spanning from nucleotide 439 through nucleotide 441 of SEQ ID NO:1.

Translation of SEQ ID NO:6, the coding strand of nCaFlt3L<sub>1013</sub>, yields a protein of about 294 amino acids, denoted herein as PCaFlt3L<sub>294</sub>, the amino acid sequence of which is presented in SEQ ID NO:7, assuming an open reading frame having an initiation codon spanning from nucleotide 35 through nucleotide 37 of SEQ ID NO:6 and a stop codon spanning from nucleotide 917 through nucleotide 919 of SEQ ID NO:6.

Translation of SEQ ID NO:43, the coding strand for nFeFlt3L<sub>942</sub>, yields a protein of about 291 amino acids, denoted herein as PFeFlt3L<sub>291</sub>, the amino acid sequence of which is presented in SEQ ID NO:44, assuming an open reading frame having an initiation codon spanning from nucleotide 31 through nucleotide 33 of SEQ ID NO:43 and a stop codon spanning from nucleotide 904 through nucleotide 906 of SEQ ID NO:43.

Translation of SEQ ID NO:52, the coding strand for nCaCD40<sub>1425</sub>, yields a protein of about 274 amino acids, denoted herein as PCaCD40<sub>274</sub>, the amino acid sequence of which is presented in SEQ ID NO:53, assuming an open reading frame having an initiation codon spanning from nucleotide 196 through nucleotide 198 of SEQ ID NO:52 and a stop codon spanning from about nucleotide 1018 through nucleotide 1020 of SEQ ID NO:52.

Translation of SEQ ID NO:60, the coding strand for nFeCD40<sub>336</sub>, yields a protein of about 112 amino acids, denoted herein as PFeCD40<sub>112</sub>, the amino acid sequence of which is presented in SEQ ID NO:61, assuming an open reading frame having an initiation codon spanning from nucleotide 1 through nucleotide 3 of SEQ ID NO:60.

Translation of SEQ ID NO:64, the coding strand for nCaCD154<sub>1878</sub>, yields a protein of about 260 amino acids, denoted herein as PCaCD154<sub>260</sub>, the amino acid

sequence of which is presented in SEQ ID NO:65, assuming an open reading frame having an initiation codon spanning from nucleotide 284 through nucleotide 286 of SEQ ID NO:64 and a stop codon spanning from nucleotide 1064 through nucleotide 1066 of SEQ ID NO:64.

5 Translation of SEQ ID NO:72, the coding strand for nFeCD154<sub>885</sub>, yields a protein of about 260 amino acids, denoted herein as PFeCD154<sub>260</sub>, the amino acid sequence of which is presented in SEQ ID NO:73, assuming an open reading frame having an initiation codon spanning from nucleotide 29 through nucleotide 31 of SEQ ID NO:72, and a stop codon spanning from nucleotide 809 through nucleotide 811 of SEQ ID

10 NO:72.

Translation of SEQ ID NO:80, the coding strand for nCaIL-5<sub>610</sub>, yields a protein of about 134 amino acids, denoted herein as PCaIL-5<sub>134</sub>, the amino acid sequence of which is presented in SEQ ID NO:81, assuming an open reading frame having an initiation codon spanning from nucleotide 29 through nucleotide 31 of SEQ ID NO:80, and a stop

15 codon spanning from nucleotide 431 through nucleotide 433 of SEQ ID NO:80.

Translation of SEQ ID NO:91, the coding strand for nCaIL-13<sub>1302</sub>, yields a protein of about 131 amino acids, denoted herein as PCaIL-13<sub>131</sub>, the amino acid sequence of which is presented in SEQ ID NO:92, assuming an open reading frame having an initiation codon spanning from nucleotide 52 through nucleotide 54 of SEQ ID NO:91

20 and a stop codon spanning from nucleotide 445 through nucleotide 447 of SEQ ID NO:91.

Translation of SEQ ID NO:107, the coding strand for nFeIFN $\alpha$ <sub>567a</sub>, yields a protein of about 189 amino acids, denoted herein as PFeIFN $\alpha$ <sub>189a</sub>, the amino acid sequence of

which is presented in SEQ ID NO:108, assuming an open reading frame having an initiation codon spanning from nucleotide 1 through nucleotide 3 and a last codon prior to a stop codon spanning from nucleotide 565 through nucleotide 567 of SEQ ID NO:107.

Translation of SEQ ID NO:110, the coding strand for nFeIFN $\alpha_{567b}$ , yields a protein of about 189 amino acids, denoted herein as PFeIFN $\alpha_{189b}$ , the amino acid sequence of which is presented in SEQ ID NO:111, assuming an open reading frame having an initiation codon spanning from nucleotide 1 through nucleotide 3 and a last codon prior to a stop codon spanning from nucleotide 565 through nucleotide 567 of SEQ ID NO:110.

Translation of SEQ ID NO:155, the coding strand for nFeIFN $\alpha_{567c}$ , yields a protein of about 189 amino acids, denoted herein as PFeIFN $\alpha_{189c}$ , the amino acid sequence of which is presented in SEQ ID NO:156, assuming an open reading frame having an initiation codon spanning from nucleotide 1 through nucleotide 3 and a last codon prior to a stop codon spanning from nucleotide 565 through nucleotide 567 of SEQ ID NO:155.

Translation of SEQ ID NO:161, the coding strand for nFeIFN $\alpha_{582d}$ , yields a protein of about 194 amino acids, denoted herein as PFeIFN $\alpha_{194d}$ , the amino acid sequence of which is presented in SEQ ID NO:162, assuming an open reading frame having an initiation codon spanning from nucleotide 1 through nucleotide 3 and a last codon prior to a stop codon spanning from nucleotide 565 through nucleotide 567 of SEQ ID NO:161.

Translation of SEQ ID NO:167, the coding strand for nFeIFN $\alpha_{567e}$ , yields a protein of about 189 amino acids, denoted herein as PFeIFN $\alpha_{189e}$ , the amino acid sequence of which is presented in SEQ ID NO:168, assuming an open reading frame having an

initiation codon spanning from nucleotide 1 through nucleotide 3 and a last codon prior to a stop codon spanning from nucleotide 565 through nucleotide 567 of SEQ ID NO:167.

Translation of SEQ ID NO:119, the coding strand for nFeGMCSF<sub>444</sub>, yields a protein of about 144 amino acids, denoted herein as PFeGMCSF<sub>144</sub>, the amino acid sequence of which is presented in SEQ ID NO:120, assuming an open reading frame having an initiation codon spanning from nucleotide 10 through nucleotide 12 of SEQ ID NO:119 and a stop codon spanning from nucleotide 442 through nucleotide 444 of SEQ ID NO:119.

Preferred IL-4 proteins of the present invention include proteins that are at least about 85%, preferably at least about 90%, and even more preferably at least about 95% identical to PCaIL-4<sub>132</sub>, PCaIL-4<sub>108</sub>, or fragments thereof. Preferred Flt-3 ligand proteins of the present invention include proteins that are at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to PCaFlt3L<sub>294</sub>, PCaFlt3L<sub>268</sub>, PCaFlt3L<sub>276</sub>, PCaFlt3L<sub>250</sub>, PCaFlt3L<sub>31</sub>, and/or fragments thereof. Additional preferred Flt-3 ligand proteins of the present invention includes proteins that are at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to PFeFlt3L<sub>291</sub>, PFeFlt3L<sub>265</sub> and/or fragments thereof. Preferred CD40 proteins of the present invention includes proteins that are at least about 70%, preferably at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to PCaCD40<sub>274</sub>, PCaCD40<sub>255</sub> and/or fragments thereof. Additional

preferred CD40 proteins of the present invention includes proteins that are at least about 60%, at least about 65%, preferably at least about 70%, preferably at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical

5 to PFeCD40<sub>112</sub> and/or fragments thereof. Preferred CD154 proteins of the present invention includes proteins that are at least about 80% identical, preferably at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to PCaCD154<sub>260</sub>, PCaCD154<sub>211</sub> and/or fragments thereof. Additional preferred CD154 proteins of the present invention includes proteins that are at least about

10 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to PFeCD154<sub>260</sub>, PFeCD154<sub>211</sub> and/or fragments thereof. Preferred IL-5 proteins of the present invention includes proteins that are at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to PCaIL-5<sub>134</sub>, PCaIL-5<sub>115</sub> and/or fragments thereof. Preferred IL-13

15 proteins of the present invention includes proteins that are at least about 70% identical, preferably at least about 75% identical, more preferably at least about 80% identical, more preferably at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to PCaIL-13<sub>131</sub>, PCaIL-13<sub>111</sub>, PCaIL-13<sub>130</sub>, PCaIL-13<sub>110</sub>, and/or fragments thereof. Preferred IFN $\alpha$  proteins of the

20 present invention include PFeIFN $\alpha$ <sub>189a</sub>, PFeIFN $\alpha$ <sub>189b</sub>, PFeIFN $\alpha$ <sub>189c</sub>, PFeIFN $\alpha$ <sub>166a</sub>, PFeIFN $\alpha$ <sub>166c</sub>, PFeIFN $\alpha$ <sub>194d</sub>, PFeIFN $\alpha$ <sub>171d</sub>, PFeIFN $\alpha$ <sub>189e</sub>, PFeIFN $\alpha$ <sub>166e</sub>, and/or PFeIFN $\alpha$ <sub>166b</sub>. Preferred GM-CSF proteins of the present invention include PFeGMCSF<sub>144</sub>, and/or PFeGMCSF<sub>127</sub>.

More preferred are IL-4 proteins comprising PCaIL-4<sub>132</sub>, PCaIL-4<sub>108</sub>, and/or proteins encoded by allelic variants of a nucleic acid molecule encoding proteins PCaIL-4<sub>132</sub> and/or PCaIL-4<sub>108</sub>. More preferred are Flt-3 ligand proteins comprising PCaFlt3L<sub>294</sub>, PCaFlt3L<sub>268</sub>, PCaFlt3L<sub>276</sub>, PCaFlt3L<sub>250</sub>, PCaFlt3L<sub>31</sub>, PFeFlt3L<sub>291</sub>, PFeFlt3L<sub>265</sub> and/or proteins encoded by allelic variants of a nucleic acid molecule encoding proteins PCaFlt3L<sub>294</sub>, PCaFlt3L<sub>268</sub>, PCaFlt3L<sub>276</sub>, PCaFlt3L<sub>250</sub>, PCaFlt3L<sub>31</sub>, PFeFlt3L<sub>291</sub>, and/or PFeFlt3L<sub>265</sub>. More preferred are CD40 proteins comprising PCaCD40<sub>274</sub>, PCaCD40<sub>255</sub>, and/or PFeCD40<sub>112</sub> and/or proteins encoded by allelic variants of a nucleic acid molecule encoding proteins PCaCD40<sub>274</sub>, PCaCD40<sub>255</sub>, and/or PFeCD40<sub>112</sub>. More preferred are CD154 proteins comprising PCaCD154<sub>260</sub>, PCaCD154<sub>211</sub>, PFeCD154<sub>260</sub>, PFeCD154<sub>211</sub> and/or proteins encoded by allelic variants of a nucleic acid molecule encoding one of proteins PCaCD154<sub>260</sub>, PCaCD154<sub>211</sub>, PFeCD154<sub>260</sub>, PFeCD154<sub>211</sub>. More preferred are IL-5 proteins comprising PCaIL-5<sub>134</sub>, PCaIL-5<sub>115</sub> and/or proteins encoded by allelic variants of a nucleic acid molecule encoding one of the proteins PCaIL-5<sub>134</sub> and/or PCaIL-5<sub>115</sub>. More preferred are IL-13 proteins comprising PCaIL-13<sub>131</sub>, PCaIL-13<sub>111</sub>, PCaIL-13<sub>130</sub>, PCaIL-13<sub>110</sub>, and/or proteins encoded by allelic variants of a nucleic acid molecule encoding one of the proteins PCaIL-13<sub>131</sub>, PCaIL-13<sub>111</sub>, PCaIL-13<sub>130</sub>, PCaIL-13<sub>110</sub>.

Also preferred are IL-4 proteins of the present invention having amino acid sequences that are at least about 85%, preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:2, SEQ ID NO:20 and/or fragments thereof. Also preferred are Flt-3 ligand proteins of the present invention having amino acid sequences that are at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even



more preferably at least about 95% identical to SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34 and/or fragments thereof. Additional preferred Flt-3 ligand proteins of the present invention includes proteins that are at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and/or even more preferably at least about 95% identical to SEQ ID NO:44, SEQ ID NO:49 and/or fragments thereof. Preferred CD40 proteins of the present invention includes proteins that are at least about 70%, preferably at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and/or even more preferably at least about 95% identical to SEQ ID NO:53, SEQ ID NO:58 and/or fragments thereof. Additional preferred CD40 proteins of the present invention includes proteins that are at least about 60%, at least about 65%, preferably at least about 70%, preferably at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:61 and/or fragments thereof. Preferred CD154 proteins of the present invention includes proteins that are at least about 80% identical, preferably at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:65, SEQ ID NO:70 and/or fragments thereof. Additional preferred CD154 proteins of the present invention includes proteins that are at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:73, SEQ ID NO:78 and/or fragments thereof. Preferred IL-5 proteins of the present invention includes proteins that are at least about 85% identical, even more preferably at

least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:81, SEQ ID NO:86 and/or fragments thereof. Preferred IL-13 proteins of the present invention includes proteins that are at least about 70% identical, preferably at least about 75% identical, more preferably at least about 80% identical, more preferably at least about 85% identical, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, SEQ ID NO:105, and/or fragments thereof. Preferred IFN $\alpha$  proteins of the present invention include SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and SEQ ID NO:171. Preferred GM-CSF proteins of the present invention include SEQ ID NO:120, SEQ ID NO:125.

More preferred are IL-4 proteins comprising the amino acid sequence SEQ ID NO:2, SEQ ID NO:20; and/or IL-4 proteins encoded by allelic variants of nucleic acid molecules encoding IL-4 proteins having the amino acid sequence SEQ ID NO:2, SEQ ID NO:20. More preferred are Flt-3 ligand proteins comprising SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34, SEQ ID NO:44, SEQ ID NO:49 and/or proteins encoded by allelic variants of a nucleic acid molecule encoding proteins SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:44, and/or SEQ ID NO:49. More preferred are CD40 proteins comprising SEQ ID NO:53, SEQ ID NO:58, SEQ ID NO:61 and/or proteins encoded by allelic variants of a nucleic acid molecule encoding proteins SEQ ID NO:53, SEQ ID NO:58, and/or SEQ ID NO:61. More preferred are CD154 proteins comprising SEQ ID NO:65, SEQ ID NO:70, SEQ ID NO:73, SEQ ID NO:78 and/or proteins encoded by allelic

variants of a nucleic acid molecule encoding one of proteins SEQ ID NO:65, SEQ ID NO:70, SEQ ID NO:73, and/or SEQ ID NO:78. More preferred are IL-5 proteins comprising SEQ ID NO:81, SEQ ID NO:86 and/or proteins encoded by allelic variants of a nucleic acid molecule encoding one of the proteins SEQ ID NO:81, and/or SEQ ID NO:86. More preferred are IL-13 proteins comprising SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, SEQ ID NO:105, and/or proteins encoded by allelic variants of a nucleic acid molecule encoding one of the proteins SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105.

Percent identities between amino acid or nucleic acid sequences can be determined using standard methods known to those of skill in the art. It is known in the art that methods to determine the percentage identity and the number of gaps are substantially similar when different methods for determining sequence similarity are used and when the degree of similarity is greater than 30% amino acid identity, as described by Johnson et al., *J. Mol. Biol.*, vol. 233, pages 716-738, 1993, and Feng et al., *J. Mol. Evol.*, vol. 21, pages 112-125, 1985, which are incorporated by reference herein in their entirety. Preferred methods to determine percentage identities between amino acid sequences and between nucleic acid sequences include comparisons using various computer programs such as GCG<sup>TM</sup> program (available from Genetics Computer Group, Madison, WI), DNAsis<sup>TM</sup> program (available from Hitachi Software, San Bruno, CA) or the MacVector<sup>TM</sup> program (available from the Eastman Kodak Company, New Haven, CT). Preferred settings for sequence comparisons using the DNAsis<sup>TM</sup> computer program or the GAP GCG<sup>TM</sup> program are disclosed herein in the Examples section.

Additional preferred IL-4 proteins of the present invention include proteins encoded by nucleic acid molecules comprising at least a portion of nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, and/or nCaIL-4<sub>324</sub>, as well as IL-4 proteins encoded by allelic variants of such nucleic acid molecules. Additional preferred Flt-3 ligand proteins of the present invention include proteins encoded by nucleic acid molecules comprising at least a portion of nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>, nCaFlt3L<sub>985</sub>, nCaFlt3L<sub>1019</sub>, nCaFlt3L<sub>93</sub>, nCaFlt3L<sub>750</sub>, nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>, nFeFlt3L<sub>873</sub>, and/or nFeFlt3L<sub>795</sub> as well as Flt-3 ligand proteins encoded by allelic variants of such nucleic acid molecules. Additional preferred CD40 proteins of the present invention include proteins encoded by nucleic acid molecules encoding at least a portion of nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, nCaCD40<sub>765</sub>, and/or nFeCD40<sub>336</sub> as well as CD40 proteins encoded by allelic variants of such nucleic acid molecules. Additional preferred CD154 proteins of the present invention include proteins encoded by nucleic acid molecules encoding at least a portion of nCaCD154<sub>390</sub>, nCaCD154<sub>1878</sub>, nCaCD154<sub>780</sub>, nCaCD154<sub>633</sub>, nFeCD154<sub>885</sub>, nFeCD154<sub>780</sub>, and/or nFeCD154<sub>633</sub> as well as CD154 proteins encoded by allelic variants of such nucleic acid molecules. Additional preferred IL-5 proteins of the present invention include proteins encoded by nucleic acid molecules encoding at least a portion of nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, and/or nCaIL-5<sub>345</sub> as well as IL-5 proteins encoded by allelic variants of such nucleic acid molecules. Additional preferred IL-13 proteins of the present invention include proteins encoded by nucleic acid molecules encoding at least a portion of nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, and/or nCaIL-5<sub>345</sub> as well as IL-13 proteins encoded by allelic variants of such nucleic acid molecules.

Also preferred are IL-4 proteins encoded by nucleic acid molecules having nucleic acid sequences comprising at least a portion of SEQ ID NO:1, SEQ ID NO:4, and/or SEQ ID NO:19, as well as allelic variants of these nucleic acid molecules. Also preferred are Flt-3 ligand proteins encoded by nucleic acid molecules having nucleic acid sequences

5 comprising at least a portion of SEQ ID NO:6, SEQ ID NO:9, SEQ ID NO:22, SEQ ID NO:25, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:33, SEQ ID NO:36, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:46, and/or SEQ ID NO:48, as well as allelic variants of these nucleic acid molecules. Also preferred are CD40 proteins encoded by nucleic acid molecules having nucleic acid sequences comprising at least a

10 portion of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, SEQ ID NO:57, and/or SEQ ID NO:60, as well as allelic variants of these nucleic acid molecules. Also preferred are CD154 proteins encoded by nucleic acid molecules having nucleic acid sequences comprising at least a portion of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, SEQ ID NO:69, SEQ ID NO:72, SEQ ID NO:75, and/or SEQ ID NO:77, as well as allelic variants

15 of these nucleic acid molecules. Also preferred are IL-5 proteins encoded by nucleic acid molecules having nucleic acid sequences comprising at least a portion of SEQ ID NO:80, SEQ ID NO:83, and/or SEQ ID NO:85, as well as allelic variants of these nucleic acid molecules. Also preferred are IL-13 proteins encoded by nucleic acid molecules having nucleic acid sequences comprising at least a portion of SEQ ID NO:88, SEQ ID NO:89,

20 SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, and/or SEQ ID NO:104, as well as allelic variants of these nucleic acid molecules.

Another embodiment of the present invention is a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecule that includes one or more regulatory regions, full-length or partial coding regions, or combinations thereof. The minimal size of a nucleic acid molecule of the present invention is a size sufficient to allow the formation of a stable hybrid (i.e., hybridization under stringent hybridization conditions) with the complementary sequence of another nucleic acid molecule. As such, the minimal size of a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecule of the present invention is from about 12 to about 18 nucleotides in length.

In accordance with the present invention, an isolated nucleic acid molecule is a nucleic acid molecule that has been removed from its natural milieu (i.e., that has been subjected to human manipulation) and can include DNA, RNA, or derivatives of either DNA or RNA. As such, "isolated" does not reflect the extent to which the nucleic acid molecule has been purified. An isolated canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecule of the present invention can be isolated from its natural source or produced using recombinant DNA technology (e.g., polymerase chain reaction (PCR) amplification or cloning) or chemical synthesis. Isolated canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, and/or feline GM-CSF, nucleic acid molecules can include, for example,

natural allelic variants and/or nucleic acid molecules modified by nucleotide insertions, deletions, substitutions, and/or inversions in a manner such that the modifications do not substantially interfere with the nucleic acid molecule's ability to encode an canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline  
 5 CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, and/or feline GM-CSF protein of the present invention.

A canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, and/or feline GM-CSF ligand nucleic acid molecule homolog can be produced  
 10 using a number of methods known to those skilled in the art, see, for example, Sambrook et al., 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Labs Press; Sambrook et al., *ibid.*, is incorporated by reference herein in its entirety. For example, nucleic acid molecules can be modified using a variety of techniques including, but not limited to, classic mutagenesis and recombinant DNA techniques such as site-directed  
 15 mutagenesis, chemical treatment, restriction enzyme cleavage, ligation of nucleic acid fragments, PCR amplification, synthesis of oligonucleotide mixtures and ligation of mixture groups to "build" a mixture of nucleic acid molecules, and combinations thereof. Nucleic acid molecule homologs can be selected by hybridization with either a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline  
 20 CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecule or by screening the function of a protein encoded by the nucleic acid molecule (e.g., ability to elicit an immune response against at least one epitope of a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40,



canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, respectively).

An isolated nucleic acid molecule of the present invention can include a nucleic acid sequence that encodes at least one canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein of the present invention, examples of such proteins being disclosed herein. Although the phrase “nucleic acid molecule” primarily refers to the physical nucleic acid molecule and the phrase “nucleic acid sequence” primarily refers to the sequence of nucleotides on the nucleic acid molecule, the two phrases can be used interchangeably, especially with respect to a nucleic acid molecule, or a nucleic acid sequence, being capable of encoding a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF ligand protein.

A preferred nucleic acid molecule of the present invention, when administered to an animal, is capable of regulating an immune response in an animal. As will be disclosed in more detail below, such a nucleic acid molecule can be, or encode, an antisense RNA, a molecule capable of triple helix formation, a ribozyme, or other nucleic acid-based drug compound. In additional embodiments, a nucleic acid molecule of the present invention can encode an immunoregulatory protein (e.g., a cell-bound or soluble protein of the present invention), the nucleic acid molecule being delivered to the animal, for example, by direct injection (i.e, as a genetic vaccine) or in a vehicle such as a recombinant virus vaccine or a recombinant cell vaccine.

One embodiment of the present invention is an IL-4 nucleic acid molecule comprising all or part (i.e., a fragment of the IL-4 nucleic acid molecule) of nucleic acid molecules nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, and/or nCaIL-4<sub>324</sub>, or allelic variants of these nucleic acid molecules. One embodiment of the present invention is a Flt-3 ligand nucleic acid molecule comprising all or part (i.e., a fragment of the Flt-3 ligand nucleic acid molecule) of nucleic acid molecules nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>, nCaFlt3L<sub>985</sub>, nCaFlt3L<sub>1019</sub>, nCaFlt3L<sub>93</sub>, nCaFlt3L<sub>750</sub>, nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>, nFeFlt3L<sub>873</sub>, and/or nFeFlt3L<sub>795</sub> and/or allelic variants of these nucleic acid molecules.

One embodiment of the present invention is a CD40 nucleic acid molecule comprising all or part (i.e. a fragment of the CD40 nucleic acid molecule) of nucleic acid molecules nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, nCaCD40<sub>765</sub>, and/or nFeCD40<sub>336</sub> and/or allelic variants of these nucleic acid molecules. One embodiment of the present invention is a CD154 nucleic acid molecule comprising all or part of nucleic acid molecules nCaCD154<sub>390</sub>, nCaCD154<sub>1878</sub>, nCaCD154<sub>780</sub>, nCaCD154<sub>633</sub>, nFeCD154<sub>885</sub>, nFeCD154<sub>780</sub>, and/or nFeCD154<sub>633</sub>, and/or allelic variants of these nucleic acid molecules. One embodiment of the present invention is an IL-5 nucleic acid molecule comprising all or part of nucleic acid molecules nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, and/or nCaIL-5<sub>345</sub>, and/or allelic variants of these nucleic acid molecules. One embodiment of the present invention is an IL-13 nucleic acid molecule comprising all or part of nucleic acid molecules nCaIL-13<sub>166</sub>, nCaIL-13<sub>272</sub>, nCaIL-13<sub>278</sub>, nCaIL-13<sub>1302</sub>, nCaIL-13<sub>393</sub>, nCaIL-13<sub>333</sub>, nCaIL-13<sub>1269</sub>, nCaIL-13<sub>390</sub>, and/or nCaIL-13<sub>330</sub>, and/or allelic variants of these nucleic acid molecules. Another preferred nucleic acid molecule of the present invention includes at least a portion of (i.e., a fragment of the nucleic acid molecule) nucleic acid sequence SEQ ID NO:1, SEQ ID

NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:6,  
 SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID  
 NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID  
 NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID  
 5 NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID  
 NO:47, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID  
 NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:59, SEQ ID  
 NO:60, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID  
 NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:72, SEQ ID  
 10 NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID  
 NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID  
 NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID  
 NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID  
 NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID  
 15 NO:106, SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID  
 NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:119, SEQ ID  
 NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:126, SEQ ID  
 NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID  
 NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID  
 20 NO:170, and/or SEQ ID NO:172, as well as allelic variants of nucleic acid molecules  
 having these nucleic acid sequences. Such nucleic acid molecules can include  
 nucleotides in addition to those included in the SEQ ID NOs, such as, but not limited to, a

full-length gene, a full-length coding region, a nucleic acid molecule encoding a fusion protein, and/or a nucleic acid molecule encoding a multivalent therapeutic compound.

One embodiment of an isolated nucleic acid molecule of the present invention is a nucleic acid molecule that can be any of the following: (a) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21 and/or a homolog thereof, wherein said homolog has an at least 50 contiguous nucleotide region identical in sequence to a 50 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21; (b) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37, and/or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a 40 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37; (c) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or SEQ ID NO:50, and/or a

homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or SEQ ID NO:50; (d) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or SEQ ID NO:59, and/or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a 40 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or SEQ ID NO:59; (e) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and/or SEQ ID NO:62, and/or a homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and/or SEQ ID NO:62; (f) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69 and/or SEQ ID NO:71, and/or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ

ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69 and/or SEQ ID NO:71; (g) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79, and/or a

5 homolog thereof, wherein said homolog has an at least 35 contiguous nucleotide region identical in sequence to a 35 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79;

(h) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from

10 the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and/or SEQ ID NO:87, and/or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID

15 NO:84, SEQ ID NO:85, and/or SEQ ID NO:87; (i) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106, and/or a homolog

20 thereof, wherein said homolog has an at least 15 contiguous nucleotide region identical in sequence to a 15 contiguous nucleotide region of a nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89,

SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106; (j) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170 and/or SEQ ID NO:172; and/or (k) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, and/or SEQ ID NO:126. The phrase, a homolog having an at least “x” contiguous nucleotide region identical in sequence to an “x” contiguous nucleotide region of a nucleic acid molecule selected from the group consisting of SEQ ID NO:“y”, refers to an “x”-nucleotide in length nucleic acid molecule that is identical in sequence to an “x”-nucleotide portion of SEQ ID NO:“y”, as well as to nucleic acid molecules that are longer in length than “x”. The additional length may be in the form of nucleotides that extend from either the 5' or the 3' end(s) of the contiguous identical “x”-nucleotide portion. The 5' and/or 3' extensions can include one or more extensions that have no identity to an immunoregulatory molecule of the present invention, as well as extensions that show similarity or identity to cited nucleic acids sequences or portions thereof.

In another embodiment, an isolated nucleic acid molecule of the present invention can be any of the following: (a) a nucleic acid molecule having a nucleic acid sequence



encoding an IL-4 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20 and/or (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence

5 selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20; (b) a nucleic acid molecule having a nucleic acid sequence encoding a Flt-3 ligand protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID

10 NO:34, and/or (ii) a protein comprising a fragment of at least 25 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34; (c) a nucleic acid molecule having a nucleic acid sequence encoding a Flt-3 ligand protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 75 percent identical to

15 an amino acid sequence selected from the group consisting of SEQ ID NO:44 and/or SEQ ID NO:49 and/or (ii) a protein comprising a fragment of at least 25 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:44 and/or SEQ ID NO:49; (d) a nucleic acid molecule having a nucleic acid sequence encoding a CD40 protein selected from the group consisting of (i) a protein having an amino acid sequence

20 that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:53 and/or SEQ ID NO:58 and/or (ii) a protein comprising a fragment of at least 30 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:53 and/or SEQ ID NO:58; (e) a nucleic acid

molecule having a nucleic acid sequence encoding a CD40 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 60 percent identical to an amino acid sequence comprising SEQ ID NO:61 and/or (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence comprising SEQ ID NO:61; (f) a nucleic acid molecule having a nucleic acid sequence encoding a CD154 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 80 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:65 and/or SEQ ID NO:70, and/or (ii) a protein comprising a fragment of at least 35 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:65 and/or SEQ ID NO:70; (g) a nucleic acid molecule having a nucleic acid sequence encoding a CD154 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:73 and/or SEQ ID NO:78, and/or (ii) a protein comprising a fragment of at least 50 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:73 and/or SEQ ID NO:78; (h) a nucleic acid molecule having a nucleic acid sequence encoding an IL-5 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86 and/or (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86; (i) a nucleic acid molecule having a nucleic acid sequence encoding an IL-13 protein selected from the group consisting of (i) a protein having an amino acid sequence that is

at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105 and/or (ii) a protein comprising a fragment of at least 15 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or SEQ ID NO:105; (j) a nucleic acid molecule having a nucleic acid sequence encoding an interferon alpha protein having an amino acid sequence that is selected from the group consisting of amino acid sequence SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and/or SEQ ID NO:171; (k) a nucleic acid molecule having a nucleic acid sequence encoding a GMCSF protein having an amino acid sequence that is selected from the group consisting of amino acid sequence SEQ ID NO:120, SEQ ID NO:125, and/or (l) a nucleic acid molecule comprising a complement of any of the before-mentioned nucleic acid sequences; wherein said IL-4 protein elicits an immune response against an IL-4 protein selected from the group consisting of SEQ ID NO:2 and/or SEQ ID NO:20 and/or is a protein with interleukin-4 activity, said Flt-3 ligand protein elicits an immune response against a Flt-3 ligand protein selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:44, and/or SEQ ID NO:49 and/or is a protein with Flt-3 ligand activity, said CD40 protein elicits an immune response against a CD40 protein selected from the group consisting of SEQ ID NO:53, SEQ ID NO:58, and/or SEQ ID NO:61 and/or is a protein with CD40 activity, said CD154 protein elicits an immune response against a CD154 protein selected from the group consisting of SEQ ID NO:65, SEQ ID NO:70, SEQ ID NO:73, and/or SEQ ID NO:78 and/or is a protein with CD154 activity,

said IL-5 protein elicits an immune response against a IL-5 protein selected from the group consisting of SEQ ID NO:81 and/or SEQ ID NO:86 and/or is a protein with IL-5 activity, said IL-13 protein elicits an immune response against an IL-13 protein selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and/or  
 5 SEQ ID NO:105 and/or is a protein with IL-13 activity, said interferon alpha protein elicits an immune response against an interferon alpha protein selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and/or SEQ ID NO:171 and/or is a protein with interferon alpha activity, and said  
 10 GMCSF protein elicits an immune response against a GMCSF protein selected from the group consisting of SEQ ID NO:120 and/or SEQ ID NO:125 and/or is a protein with GM-CSF activity.

In one embodiment, an IL-4 nucleic acid molecule of the present invention encodes a protein that is at least about 85%, preferably at least about 90%, preferably at  
 15 least about 92%, and even more preferably at least about 95% identical to PCaIL-4<sub>132</sub> and/or PCaIL-4<sub>108</sub>. In one embodiment, a Flt-3 ligand nucleic acid molecule of the present invention encodes a protein that is at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to PCaFlt3L<sub>294</sub>,  
 20 PCaFlt3L<sub>268</sub>, PCaFlt3L<sub>276</sub>, PCaFlt3L<sub>250</sub>, and/or PCaFlt3L<sub>31</sub>. In one embodiment, a Flt-3 ligand nucleic acid molecule of the present invention encodes a protein that is at least about 75%, more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95%

identical to PFeFlt3L<sub>291</sub>, and/or PFeFlt3L<sub>265</sub>. In one embodiment, a CD40 nucleic acid molecule of the present invention encodes a protein that is at least about PCaCD40<sub>274</sub>, and/or PCaCD40<sub>255</sub>. In one embodiment, a CD40 nucleic acid molecule of the present invention encodes a protein that is at least about 60%, preferably at least about 65%,  
 5 preferably at least about 70%, preferably at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to PFeCD40<sub>112</sub>. In one embodiment, a CD154 nucleic acid molecule of the present invention encodes a protein that is at least about 80%, at least about 85%, more preferably at least about 90%, and  
 10 even more preferably at least about 95% identical to PCaCD154<sub>260</sub>, and/or PCaCD154<sub>211</sub>. In one embodiment, a CD154 nucleic acid molecule of the present invention encodes a protein that is at least about 85%, more preferably at least about 90%, and even more preferably at least about 95% identical to PFeCD154<sub>260</sub>, PFeCD154<sub>211</sub>. In one  
 15 embodiment, an IL-5 nucleic acid molecule of the present invention encodes a protein that is at least about 85%, more preferably at least about 90%, and even more preferably at least about 95% identical to PCaIL-5<sub>134</sub>, and/or PCaIL-5<sub>115</sub>. In one embodiment, an IL-13 nucleic acid molecule of the present invention encodes a protein that is at least about 70%, at least about 75%, at least about 80%, preferably at least about 85%, more  
 20 preferably at least about 90%, and even more preferably at least about 95% identical to PCaIL-13<sub>131</sub>, PCaIL-13<sub>111</sub>, PCaIL-13<sub>130</sub>, PCaIL-13<sub>110</sub>. Even more preferred is a nucleic acid molecule encoding PCaIL-4<sub>132</sub>, PCaIL-4<sub>108</sub>, PCaFlt3L<sub>294</sub>, PCaFlt3L<sub>268</sub>, PCaFlt3L<sub>276</sub>, PCaFlt3L<sub>250</sub>, PCaFlt3L<sub>31</sub>, PFeFlt3L<sub>291</sub>, PFeFlt3L<sub>265</sub>, PCaCD40<sub>274</sub>, PCaCD40<sub>255</sub>, PFeCD40<sub>112</sub>, PCaCD154<sub>260</sub>, PCaCD154<sub>211</sub>, PFeCD154<sub>260</sub>, PFeCD154<sub>211</sub>, PCaIL-5<sub>134</sub>,

PCaIL-5<sub>115</sub>, PCaIL-13<sub>131</sub>, PCaIL-13<sub>111</sub>, PCaIL-13<sub>130</sub>, PCaIL-13<sub>110</sub> and/or an allelic variant of such a nucleic acid molecule.

In another embodiment, an IL-4 nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about 85%, preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:2, SEQ ID NO:20. The present invention also includes an IL-4 nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:2, and/or SEQ ID NO:20, as well as allelic variants of an IL-4 nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a Flt-3 ligand nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34. The present invention also includes a Flt-3 ligand nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and/or SEQ ID NO:34, as well as allelic variants of a Flt-3 ligand nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a Flt-3 ligand nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about 75%, more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:44, and/or SEQ ID NO:49. The present invention also includes a Flt-3 ligand nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:44, and/or SEQ ID NO:49, as well as allelic variants of a Flt-3 ligand nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a CD40 nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about 70%, preferably at least about 75%, even more preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:53 and/or SEQ ID NO:58. The present invention also includes a CD40 nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:53 and/or SEQ ID NO:58, as well as allelic variants of a CD40 nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a CD40 nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about 60%, preferably at least about 65%, preferably at least about 70%, preferably at least about 75%, even more



preferably at least about 80%, even more preferably at least about 85%, even more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:60. The present invention also includes a CD40 nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:60, as well as allelic variants  
5 of a CD40 nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a CD154 nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about at least about 80%,  
10 at least about 85%, more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, and/or SEQ ID NO:69. The present invention also includes a CD154 nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, and/or SEQ ID NO:69, as well as allelic variants of a CD154 nucleic acid molecule  
15 encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a CD154 nucleic acid molecule of the present invention encodes a protein having an amino acid sequence that is at least about at least about 85%,  
20 more preferably at least about 90%, and even more preferably at least about 95% identical to SEQ ID NO:72, SEQ ID NO:75, and/or SEQ ID NO:77. The present invention also includes a CD154 nucleic acid molecule encoding a protein having at least a portion of SEQ ID NO:72, SEQ ID NO:75, and/or SEQ ID NO:77, as well as allelic variants of a

CD154 nucleic acid molecule encoding a protein having these sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, an IL-5 nucleic acid molecule of the present invention  
 5 encodes a protein having an amino acid sequence that is at least about at least about 85%,  
 at least about 85%, more preferably at least about 90%, and even more preferably at least  
 about 95% identical to SEQ ID NO:80, SEQ ID NO:83, and/or SEQ ID NO:85. The  
 present invention also includes an IL-5 nucleic acid molecule encoding a protein having  
 at least a portion of SEQ ID NO:80, SEQ ID NO:83, and/or SEQ ID NO:85, as well as  
 10 allelic variants of an IL-5 nucleic acid molecule encoding a protein having these  
 sequences, including nucleic acid molecules that have been modified to accommodate  
 codon usage properties of the cells in which such nucleic acid molecules are to be  
 expressed.

In another embodiment, an IL-13 nucleic acid molecule of the present invention  
 15 encodes a protein having an amino acid sequence that is at least about at least about 70%,  
 at least about 75%, at least about 80%, preferably at least about 85%, more preferably at  
 least about 90%, and even more preferably at least about 95% identical to SEQ ID  
 NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94, SEQ ID  
 NO:96, SEQ ID NO:99, SEQ ID NO:102, and/or SEQ ID NO:104. The present invention  
 20 also includes an IL-13 nucleic acid molecule encoding a protein having at least a portion  
 of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94,  
 SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, and/or SEQ ID NO:104, as well as  
 allelic variants of an IL-13 nucleic acid molecule encoding a protein having these

sequences, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In one embodiment, an IL-4 nucleic acid molecule of the present invention is at least about 90%, and preferably at least about 95% identical to nCaIL-4<sub>549</sub>. Even more preferred is a nucleic acid molecule comprising nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, nCaIL-4<sub>324</sub>, and/or an allelic variant of such a nucleic acid molecule. In another embodiment, a Flt-3 ligand nucleic acid molecule of the present invention is at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to nCaFlt3L<sub>1013</sub>. Even more preferred is a nucleic acid molecule comprising nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>, nCaFlt3L<sub>985</sub>, nCaFlt3L<sub>1019</sub>, nCaFlt3L<sub>93</sub>, and/or nCaFlt3L<sub>750</sub>, and/or an allelic variant of such a nucleic acid molecule. In one embodiment, a Flt-3 ligand nucleic acid molecule of the present invention is at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to nFeFlt3L<sub>942</sub>. Even more preferred is a nucleic acid molecule comprising nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>, nFeFlt3L<sub>873</sub>, and/or nFeFlt3L<sub>795</sub>, and/or an allelic variant of such a nucleic acid molecule. In one embodiment, a CD40 nucleic acid molecule of the present invention is at least about 70%, at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, and/or nCaCD40<sub>765</sub>, and/or an allelic variant of such a nucleic acid molecule. In one embodiment, a CD40 nucleic acid

molecule of the present invention is at least about 70%, at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to nFeCD40<sub>336</sub>, and/or an allelic variant of such a nucleic acid molecule. In one embodiment, a CD154

5 nucleic acid molecule of the present invention is at least about 85%, preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to nCaCD154<sub>390</sub>, nCaCD154<sub>878</sub>, nCaCD154<sub>780</sub>, and/or nCaCD154<sub>633</sub>, and/or an allelic variant of such a nucleic acid molecule. In one embodiment, a CD154

10 nucleic acid molecule of the present invention is at least about 91%, and preferably about 95% identical to nFeCD154<sub>885</sub>, nFeCD154<sub>780</sub>, and/or nFeCD154<sub>633</sub>, and/or an allelic variant of such a nucleic acid molecule. In one embodiment, an IL-5 molecule of the present invention is at least about 90% and preferably at least about 95% identical to nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, and/or nCaIL-5<sub>345</sub>, and/or an allelic variant of such a nucleic acid molecule. In another embodiment, an IL-13 molecule of the present invention is at least

15 about 65%, at least about 70%, preferably at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to nCaIL-13<sub>166</sub>, nCaIL-13<sub>272</sub>, nCaIL-13<sub>278</sub>, nCaIL-13<sub>1302</sub>, nCaIL-13<sub>393</sub>, nCaIL-13<sub>333</sub>, nCaIL-13<sub>1269</sub>, nCaIL-13<sub>390</sub>, and/or nCaIL-13<sub>330</sub>, and/or an allelic variant of such a nucleic acid molecule.

20 In another embodiment, an IL-4 nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 90%, and preferably at least about 95% identical to SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21. The present invention also includes an IL-4 nucleic acid

molecule comprising at least a portion of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and/or SEQ ID NO:21, as well as allelic variants of such IL-4 nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In another embodiment, a Flt-3 ligand nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 75%, preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37. The present invention also includes a Flt-3 ligand- nucleic acid molecule comprising at least a portion of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and/or SEQ ID NO:37, as well as allelic variants of such Flt-3 ligand nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In one embodiment, a Flt-3 ligand nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to SEQ ID NO:41, SEQ ID NO:42,

SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or  
 SEQ ID NO:50. The present invention also includes a Flt-3 ligand- nucleic acid molecule  
 comprising at least a portion of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID  
 NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and/or SEQ ID NO:50, as well  
 5 as allelic variants of such Flt-3 ligand nucleic acid molecules, including nucleic acid  
 molecules that have been modified to accommodate codon usage properties of the cells in  
 which such nucleic acid molecules are to be expressed.

In one embodiment, a CD40 nucleic acid molecule of the present invention  
 comprises a nucleic acid sequence that is at least about 70%, at least about 75%, more  
 10 preferably at least about 80%, more preferably at least about 85%, more preferably at  
 least about 90% and even more preferably at least about 95% identical to SEQ ID NO:51,  
 SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or  
 SEQ ID NO:59. The present invention also includes a CD40 nucleic acid molecule  
 comprising at least a portion of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID  
 15 NO:55, SEQ ID NO:56, SEQ ID NO:57, and/or SEQ ID NO:59, as well as allelic variants  
 of such CD40 nucleic acid molecules, including nucleic acid molecules that have been  
 modified to accommodate codon usage properties of the cells in which such nucleic acid  
 molecules are to be expressed.

In one embodiment, a CD40 nucleic acid molecule of the present invention  
 20 comprises a nucleic acid sequence that is at least about 70%, at least about 75%, more  
 preferably at least about 80%, more preferably at least about 85%, more preferably at  
 least about 90% and even more preferably at least about 95% identical to SEQ ID NO:60  
 and/or SEQ ID NO:62. The present invention also includes a CD40 nucleic acid

molecule comprising at least a portion of SEQ ID NO:60 and/or SEQ ID NO:62, as well as allelic variants of such CD40 nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

5           In one embodiment, a CD154 nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 85%, preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, and/or SEQ ID NO:71. The present invention also includes a

10       CD154 nucleic acid molecule comprising at least a portion of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, and/or SEQ ID NO:71, as well as allelic variants of such CD154 nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

15           In one embodiment, a CD154 nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 91%, and preferably about 95% identical to SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79. The present invention also includes a CD154 nucleic acid molecule comprising at least a portion of SEQ ID NO:72, SEQ ID NO:74, SEQ ID

20       NO:75, SEQ ID NO:76, SEQ ID NO:77, and/or SEQ ID NO:79, as well as allelic variants of such CD154 nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.



In one embodiment, an IL-5 nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 90% and preferably at least about 95% identical to SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and/or SEQ ID NO:87. The present invention also includes an IL-5 nucleic acid molecule comprising at least a portion of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and/or SEQ ID NO:87, as well as allelic variants of such IL-5 nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

10 In one embodiment, an IL-13 nucleic acid molecule of the present invention comprises a nucleic acid sequence that is at least about 65%, at least about 70%, preferably at least about 75%, more preferably at least about 80%, more preferably at least about 85%, more preferably at least about 90% and even more preferably at least about 95% identical to SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106. The present invention also includes an IL-13 nucleic acid molecule comprising at least a portion of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and/or SEQ ID NO:106, as well as allelic variants of such IL-13 nucleic acid molecules, including nucleic acid molecules that have been modified to accommodate

codon usage properties of the cells in which such nucleic acid molecules are to be expressed.

In one embodiment, an IFN $\alpha$  nucleic acid molecule of the present invention is identical to SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170, and/or SEQ ID NO:172.

In another embodiment, a GM-CSF nucleic acid molecule of the present invention is identical to SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, and/or SEQ ID NO:126.

Knowing the nucleic acid sequences of certain immunoregulatory nucleic acid molecules of the present invention allows one skilled in the art to, for example, (a) make copies of those nucleic acid molecules, (b) obtain nucleic acid molecules including at least a portion of such nucleic acid molecules (e.g., nucleic acid molecules including full-length genes, full-length coding regions, regulatory control sequences, truncated coding regions), and/or (c) obtain other immunoregulatory nucleic acid molecules. Such nucleic acid molecules can be obtained in a variety of ways including screening appropriate expression libraries with antibodies of the present invention; traditional cloning techniques using oligonucleotide probes of the present invention to screen appropriate libraries; and PCR amplification of appropriate libraries or DNA using oligonucleotide primers of the present invention. Preferred libraries to screen or from which to amplify nucleic acid molecules include mammalian cDNA libraries as well as

genomic DNA libraries. Similarly, preferred DNA sources from which to amplify nucleic acid molecules include mammalian cDNA and genomic DNA. Techniques to clone and amplify genes are disclosed, for example, in Sambrook et al., *ibid*.

The present invention also includes nucleic acid molecules that are

5 oligonucleotides capable of hybridizing, under stringent hybridization conditions, with complementary regions of other, preferably longer, nucleic acid molecules of the present invention such as those comprising canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecules. Oligonucleotides of

10 the present invention can be RNA, DNA, or derivatives of either. The minimum size of such oligonucleotides is the size required for formation of a stable hybrid between an oligonucleotide and a complementary sequence on a nucleic acid molecule of the present invention. A preferred oligonucleotide of the present invention has a maximum size of about 100 nucleotides. The present invention includes oligonucleotides that can be used

15 as, for example, probes to identify nucleic acid molecules, primers to produce nucleic acid molecules, or therapeutic reagents to inhibit canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein production or activity (e.g., as antisense-, triplex formation-, ribozyme- and/or RNA drug-based reagents). The

20 present invention also includes the use of such oligonucleotides to protect animals from disease using one or more of such technologies. Appropriate oligonucleotide-containing therapeutic compositions can be administered to an animal using techniques known to those skilled in the art.

One embodiment of the present invention includes a recombinant vector, which includes at least one isolated nucleic acid molecule of the present invention, inserted into any vector capable of delivering the nucleic acid molecule into a host cell. Such a vector contains heterologous nucleic acid sequences, that is nucleic acid sequences that are not  
 5 naturally found adjacent to nucleic acid molecules of the present invention and that preferably are derived from a species other than the species from which the nucleic acid molecule(s) are derived. The vector can be either RNA or DNA, either prokaryotic or eukaryotic, and typically is a virus or a plasmid. Recombinant vectors can be used in the cloning, sequencing, and/or otherwise manipulating immunoregulatory nucleic acid  
 10 molecules of the present invention.

One type of recombinant vector, referred to herein as a recombinant molecule, comprises a nucleic acid molecule of the present invention operatively linked to an expression vector. The phrase operatively linked refers to insertion of a nucleic acid molecule into an expression vector in a manner such that the molecule is able to be  
 15 expressed when transformed into a host cell. As used herein, an expression vector is a DNA or RNA vector that is capable of transforming a host cell and of effecting expression of a specified nucleic acid molecule. Preferably, the expression vector is also capable of replicating within the host cell. Expression vectors can be either prokaryotic or eukaryotic, and are typically viruses or plasmids. Expression vectors of the present  
 20 invention include any vectors that function (i.e., direct gene expression) in recombinant cells of the present invention, including in bacterial, fungal, parasite, insect, other animal, and plant cells. Preferred expression vectors of the present invention can direct gene

expression in bacterial, yeast, insect and mammalian cells, and more preferably in the cell types disclosed herein, more preferably *in vivo*.

In particular, expression vectors of the present invention contain regulatory sequences such as transcription control sequences, translation control sequences, origins  
 5 of replication, and other regulatory sequences that are compatible with the recombinant cell and that control the expression of nucleic acid molecules of the present invention. In particular, recombinant molecules of the present invention include transcription control sequences. Transcription control sequences are sequences which control the initiation, elongation, and termination of transcription. Particularly important transcription control  
 10 sequences are those which control transcription initiation, such as promoter, enhancer, operator and repressor sequences. Suitable transcription control sequences include any transcription control sequence that can function in at least one of the recombinant cells of the present invention. A variety of such transcription control sequences are known to those skilled in the art. Preferred transcription control sequences include those which  
 15 function in bacterial, yeast, helminth and/or other endoparasite, insect and mammalian cells, such as, but not limited to, *tac*, *lac*, *trp*, *trc*, oxy-pro, omp/lpp, rrnB, bacteriophage lambda (such as lambda p<sub>L</sub> and lambda p<sub>R</sub> and fusions that include such promoters), bacteriophage T7, T7*lac*, bacteriophage T3, bacteriophage SP6, bacteriophage SP01, metallothionein, alpha-mating factor, *Pichia* alcohol oxidase, alphavirus subgenomic  
 20 promoter, antibiotic resistance gene, baculovirus, *Heliothis zea* insect virus, vaccinia virus, herpesvirus, raccoon poxvirus, other poxvirus, adenovirus, cytomegalovirus (such as immediate early promoter), simian virus 40, retrovirus, actin, retroviral long terminal repeat, Rous sarcoma virus, heat shock, phosphate and nitrate transcription control

sequences as well as other sequences capable of controlling gene expression in prokaryotic or eukaryotic cells. Additional suitable transcription control sequences include tissue-specific promoters and enhancers as well as lymphokine-inducible promoters (e.g., promoters inducible by interferons or interleukins). Transcription control

5 sequences of the present invention can also include naturally occurring transcription control sequences naturally associated with mammals, such as dog, cat, horse or human transcription control sequences.

Suitable and preferred nucleic acid molecules to include in recombinant vectors of the present invention are as disclosed herein. Preferred nucleic acid molecules to include

10 in recombinant vectors, and particularly in recombinant molecules, include nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, nCaIL-4<sub>324</sub>, nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>, nCaFlt3L<sub>985</sub>, nCaFlt3L<sub>1019</sub>, nCaFlt3L<sub>93</sub>, nCaFlt3L<sub>750</sub>, nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>, nFeFlt3L<sub>873</sub>, nFeFlt3L<sub>795</sub>, nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, nCaCD40<sub>765</sub>, nFeCD40<sub>336</sub>, nCaCD154<sub>390</sub>, nCaCD154<sub>878</sub>, nCaCD154<sub>780</sub>, nCaCD154<sub>633</sub>, nFeCD154<sub>885</sub>, nFeCD154<sub>780</sub>,

15 nFeCD154<sub>633</sub>, nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, nCaIL-5<sub>345</sub>, nCaIL-13<sub>166</sub>, nCaIL-13<sub>272</sub>, nCaIL-13<sub>278</sub>, nCaIL-13<sub>1302</sub>, nCaIL-13<sub>393</sub>, nCaIL-13<sub>333</sub>, nCaIL-13<sub>1269</sub>, nCaIL-13<sub>390</sub>, nCaIL-13<sub>330</sub>, nFeIFN $\alpha$ <sub>567a</sub>, nFeIFN $\alpha$ <sub>567b</sub>, nFeIFN $\alpha$ <sub>567c</sub>, nFeIFN $\alpha$ <sub>498a</sub>, nFeIFN $\alpha$ <sub>498b</sub>, nFeIFN $\alpha$ <sub>498c</sub>, nFeIFN $\alpha$ <sub>582d</sub>, nFeIFN $\alpha$ <sub>513d</sub>, nFeIFN $\alpha$ <sub>567e</sub>, nFeIFN $\alpha$ <sub>498e</sub>, nFeGMCSF<sub>444</sub>, nFeGMCSF<sub>432</sub>, and/or nFeGMCSF<sub>381</sub>.

20 Recombinant molecules of the present invention may also (a) contain secretory signals (i.e., signal segment nucleic acid sequences) to enable an expressed parasitic helminth protein of the present invention to be secreted from the cell that produces the protein and/or (b) contain fusion sequences which lead to the expression of nucleic acid

molecules of the present invention as fusion proteins. Examples of suitable signal segments include any signal segment capable of directing the secretion of a protein of the present invention. Preferred signal segments include, but are not limited to, tissue plasminogen activator (t-PA), interferon, interleukin, growth hormone, histocompatibility and viral envelope glycoprotein signal segments. Suitable fusion segments encoded by fusion segment nucleic acids are disclosed herein. In addition, a nucleic acid molecule of the present invention can be joined to a fusion segment that directs the encoded protein to the proteosome, such as a ubiquitin fusion segment. Eukaryotic recombinant molecules may also include intervening and/or untranslated sequences surrounding and/or within the nucleic acid sequences of nucleic acid molecules of the present invention.

Another embodiment of the present invention includes a recombinant cell comprising a host cell transformed with one or more recombinant molecules of the present invention. Transformation of a nucleic acid molecule into a cell can be accomplished by any method by which a nucleic acid molecule can be inserted into the cell. Transformation techniques include, but are not limited to, transfection, electroporation, microinjection, lipofection, adsorption, and protoplast fusion. A recombinant cell may remain unicellular or may grow into a tissue, organ or a multicellular organism. Transformed nucleic acid molecules of the present invention can remain extrachromosomal or can integrate into one or more sites within a chromosome of the transformed (i.e., recombinant) cell in such a manner that their ability to be expressed is retained. Preferred nucleic acid molecules with which to transform a cell include immunoregulatory nucleic acid molecules of the present invention disclosed herein. Particularly preferred nucleic acid molecules with which to transform a cell include



nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, nCaIL-4<sub>324</sub>, nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>,  
nCaFlt3L<sub>985</sub>, nCaFlt3L<sub>1019</sub>, nCaFlt3L<sub>93</sub>, nCaFlt3L<sub>750</sub>, nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>,  
nFeFlt3L<sub>873</sub>, nFeFlt3L<sub>795</sub>, nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, nCaCD40<sub>765</sub>,  
nFeCD40<sub>336</sub>, nCaCD154<sub>390</sub>, nCaCD154<sub>1878</sub>, nCaCD154<sub>780</sub>, nCaCD154<sub>633</sub>, nFeCD154<sub>885</sub>,  
5 nFeCD154<sub>780</sub>, nFeCD154<sub>633</sub>, nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, nCaIL-5<sub>345</sub>, nCaIL-13<sub>166</sub>, nCaIL-  
13<sub>272</sub>, nCaIL-13<sub>278</sub>, nCaIL-13<sub>1302</sub>, nCaIL-13<sub>393</sub>, nCaIL-13<sub>333</sub>, nCaIL-13<sub>1269</sub>, nCaIL-13<sub>390</sub>,  
nCaIL-13<sub>330</sub>, nFeIFN $\alpha$ <sub>567a</sub>, nFeIFN $\alpha$ <sub>567b</sub>, nFeIFN $\alpha$ <sub>567c</sub>, nFeIFN $\alpha$ <sub>498a</sub>, nFeIFN $\alpha$ <sub>498b</sub>,  
nFeIFN $\alpha$ <sub>498c</sub>, nFeIFN $\alpha$ <sub>582d</sub>, nFeIFN $\alpha$ <sub>513d</sub>, nFeIFN $\alpha$ <sub>567e</sub>, nFeIFN $\alpha$ <sub>498e</sub>, nFeGMCSF<sub>444</sub>,  
nFeGMCSF<sub>432</sub>, and/or nFeGMCSF<sub>381</sub>.

10            Suitable host cells to transform include any cell that can be transformed with a  
nucleic acid molecule of the present invention. Host cells can be either untransformed  
cells or cells that are already transformed with at least one nucleic acid molecule (e.g.,  
nucleic acid molecules encoding one or more proteins of the present invention and/or  
other proteins useful in the production of multivalent vaccines). Host cells of the present  
15 invention either can be endogenously (i.e., naturally) capable of producing  
immunoregulatory proteins of the present invention or can be capable of producing such  
proteins after being transformed with at least one nucleic acid molecule of the present  
invention. Host cells of the present invention can be any cell capable of producing at  
least one protein of the present invention, and include bacterial, fungal (including yeast),  
20 parasite (including helminth, protozoa and ectoparasite), other insect, other animal and  
plant cells. Preferred host cells include bacterial, mycobacterial, yeast, helminth, insect  
and mammalian cells. More preferred host cells include *Salmonella*, *Escherichia*,  
*Bacillus*, *Listeria*, *Saccharomyces*, *Spodoptera*, *Mycobacteria*, *Trichoplusia*, BHK (baby

hamster kidney) cells, MDCK cells (Madin-Darby canine kidney cell line), CRFK cells (Crandell feline kidney cell line), CV-1 cells (African monkey kidney cell line used, for example, to culture raccoon poxvirus), COS (e.g., COS-7) cells, chinese hamster ovary (CHO) cells, Ltk cells and Vero cells. Particularly preferred host cells are *Escherichia coli*, including *E. coli* K-12 derivatives; *Salmonella typhi*; *Salmonella typhimurium*, including attenuated strains such as UK-1<sub>03987</sub> and SR-11<sub>04072</sub>; *Spodoptera frugiperda*; *Trichoplusia ni*; BHK cells; MDCK cells; CRFK cells; CV-1 cells; COS cells; Vero cells; and non-tumorigenic mouse myoblast G8 cells (e.g., ATCC CRL 1246). Additional appropriate mammalian cell hosts include other kidney cell lines, other fibroblast cell lines (e.g., human, murine or chicken embryo fibroblast cell lines), myeloma cell lines, Chinese hamster ovary cells, mouse NIH/3T3 cells, LMTK<sup>31</sup> cells and/or HeLa cells. In one embodiment, the proteins may be expressed as heterologous proteins in myeloma cell lines employing immunoglobulin promoters.

A recombinant cell is preferably produced by transforming a host cell with one or more recombinant molecules, each comprising one or more nucleic acid molecules of the present invention operatively linked to an expression vector containing one or more transcription control sequences, examples of which are disclosed herein.

A recombinant cell of the present invention includes any cell transformed with at least one of any nucleic acid molecule of the present invention. Suitable and preferred nucleic acid molecules as well as suitable and preferred recombinant molecules with which to transfer cells are disclosed herein.

Recombinant cells of the present invention can also be co-transformed with one or more recombinant molecules including any of canine interleukin-4, canine or feline Flt-3

ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF nucleic acid molecule encoding one or more proteins of the present invention and/or one or more other nucleic acid molecules encoding other therapeutic compounds, as disclosed herein (e.g., to produce

5 multivalent vaccines).

Recombinant DNA technologies can be used to improve expression of transformed nucleic acid molecules by manipulating, for example, the number of copies of the nucleic acid molecules within a host cell, the efficiency with which those nucleic acid molecules are transcribed, the efficiency with which the resultant transcripts are

10 translated, and the efficiency of post-translational modifications. Recombinant techniques useful for increasing the expression of nucleic acid molecules of the present invention include, but are not limited to, operatively linking nucleic acid molecules to high-copy number plasmids, integration of the nucleic acid molecules into one or more host cell chromosomes, addition of vector stability sequences to plasmids, substitutions or

15 modifications of transcription control signals (e.g., promoters, operators, enhancers), substitutions or modifications of translational control signals (e.g., ribosome binding sites, Shine-Dalgarno sequences), modification of nucleic acid molecules of the present invention to correspond to the codon usage of the host cell, deletion of sequences that destabilize transcripts, and use of control signals that temporally separate recombinant

20 cell growth from recombinant enzyme production during fermentation. The activity of an expressed recombinant protein of the present invention may be improved by fragmenting, modifying, or derivatizing nucleic acid molecules encoding such a protein.

Isolated immunoregulatory proteins of the present invention can be produced in a variety of ways, including production and/or recovery of natural proteins, production and/or recovery of recombinant proteins, and/or chemical synthesis of the proteins. In one embodiment, an isolated protein of the present invention is produced by culturing a cell capable of expressing the protein under conditions effective to produce the protein, and recovering the protein. A preferred cell to culture is a recombinant cell of the present invention. Effective culture conditions include, but are not limited to, effective media, bioreactor, temperature, pH and oxygen conditions that permit protein production. An effective medium refers to any medium in which a cell is cultured to produce an immunoregulatory protein of the present invention. Such medium typically comprises an aqueous medium having assimilable carbon, nitrogen and phosphate sources, and appropriate salts, minerals, metals and other nutrients, such as vitamins. Cells of the present invention can be cultured in conventional fermentation bioreactors, shake flasks, test tubes, microtiter dishes, and petri plates. Culturing can be carried out at a temperature, pH and oxygen content appropriate for a recombinant cell. Such culturing conditions are within the expertise of one of ordinary skill in the art.

Depending on the vector and host system used for production, resultant proteins of the present invention may either remain within the recombinant cell; be secreted into the fermentation medium; be secreted into a space between two cellular membranes, such as the periplasmic space in *E. coli*; or be retained on the outer surface of a cell or viral membrane.

The phrase “recovering the protein”, as well as similar phrases, refers to collecting the whole fermentation medium containing the protein and need not imply additional

steps of separation or purification. Proteins of the present invention can be purified using a variety of standard protein purification techniques, such as, but not limited to, affinity chromatography, ion exchange chromatography, filtration, electrophoresis, hydrophobic interaction chromatography, gel filtration chromatography, reverse phase

5 chromatography, concanavalin A chromatography, chromatofocusing and/or differential solubilization. Proteins of the present invention are preferably retrieved in “substantially pure” form. As used herein, “substantially pure” refers to a purity that allows for the effective use of the protein as a therapeutic composition or diagnostic. A therapeutic composition for animals, for example, should exhibit no substantial toxicity and

10 preferably should be capable of stimulating the production of antibodies in a treated animal.

The present invention also includes isolated (i.e., removed from their natural milieu) antibodies that selectively bind to an immunoregulatory protein of the present invention and/or a mimetope thereof (e.g., anti-IL-4 antibodies, anti-Flt-3 ligand

15 antibodies, anti-CD40 antibodies, anti-CD154 antibodies, anti-IL-5 antibodies, anti-IL-13 antibodies, anti-IFN $\alpha$  antibodies, and/or anti-GM-CSF antibodies). As used herein, the term “selectively binds to” an immunoregulatory protein of the present invention, refers to the ability of antibodies of the present invention to preferentially bind to specified proteins and/or mimetopes thereof of the present invention. Binding can be measured

20 using a variety of methods standard in the art including enzyme immunoassays (e.g., ELISA), immunoblot assays, etc.; see, for example, Sambrook et al., *ibid.*, and Harlow, et al., 1988, *Antibodies, a Laboratory Manual*, Cold Spring Harbor Labs Press; Harlow et al., *ibid.*, is incorporated by this reference herein in its entirety. An anti-IL-4 antibody of

the present invention preferably selectively binds to an IL-4 protein in such a way as to inhibit the function of that protein. An anti-Flt-3 ligand antibody of the present invention preferably selectively binds to a Flt-3 ligand- protein in such a way as to inhibit the function of that protein. An anti-CD40 antibody of the present invention preferably

5 selectively binds to a CD40 protein in such a way as to inhibit the function of that protein. An anti-CD154 antibody of the present invention preferably selectively binds to a CD154 protein in such a way as to inhibit the function of that protein. An anti-IL-5 antibody of the present invention preferably selectively binds to an IL-5 protein in such a way as to inhibit the function of that protein. An anti-IL-13 antibody of the present invention

10 preferably selectively binds to an IL-13 protein in such a way as to inhibit the function of that protein. An anti-IFN $\alpha$  antibody of the present invention preferably selectively binds to an IFN $\alpha$  protein in such a way as to inhibit the function of that protein. An anti-GM-CSF antibody of the present invention preferably selectively binds to a GM-CSF protein in such a way as to inhibit the function of that protein.

15 Isolated antibodies of the present invention can include antibodies in serum, or antibodies that have been purified to varying degrees. Antibodies of the present invention can be polyclonal or monoclonal, or can be functional equivalents such as antibody fragments and/or genetically-engineered antibodies, including single chain antibodies or chimeric antibodies that can bind to one or more epitopes.

20 A preferred method to produce antibodies of the present invention includes (a) administering to an animal an effective amount of a protein, peptide and/or mimotope thereof of the present invention to produce the antibodies and (b) recovering the antibodies. In another method, antibodies of the present invention are produced

recombinantly using techniques as heretofore disclosed to produce any of the immunoregulatory proteins of the present invention. Antibodies raised against defined proteins or mimetopes can be advantageous because such antibodies are not substantially contaminated with antibodies against other substances that might otherwise cause interference in a diagnostic assay or side effects if used in a therapeutic composition.

Antibodies of the present invention have a variety of potential uses that are within the scope of the present invention. For example, such antibodies can be used (a) as reagents in assays to detect an immunoregulatory protein of the present invention, (b) as reagents in assays to modulate cellular activity through an immunoregulatory protein of the present invention (e.g., mimicking ligand binding to a canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, or feline GM-CSF protein, as appropriate), and/or (c) as tools to screen expression libraries and/or to recover desired proteins of the present invention from a mixture of proteins and other contaminants. Furthermore, antibodies of the present invention can be used to target compounds (e.g., nucleic acid molecules, drugs or proteins) to antigen presenting cells. Targeting can be accomplished by conjugating (i.e., stably joining) such antibodies to the compounds using techniques known to those skilled in the art. Suitable compounds are known to those skilled in the art.

One embodiment of the present invention is a therapeutic composition that, when administered to an animal in an effective manner, is capable of regulating an immune response in an animal. Therapeutic compositions of the present invention can include at least one of the following therapeutic compounds: an isolated IL-4, Flt-3 ligand, CD40,



CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF protein of the present invention and/or a mimetope thereof; an isolated IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF nucleic acid molecule of the present invention; an isolated antibody that selectively binds to an IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF protein of the present invention; an inhibitor of canine IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF function identified by its ability to bind to an IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF protein, respectively, of the present invention; such an inhibitor can inhibit binding of the respective immunoregulatory protein with its respective receptor, or inhibit the activity of the respective protein. Methods to perform such assays to measure binding and/or activity of an immunoregulatory protein of the present invention are known to those of skill in the art, and are described, for example, in Janeway et al., *ibid*. As used herein, a therapeutic compound refers to a compound that, when administered to an animal in an effective manner, is able to treat, ameliorate, and/or prevent a disease. Examples of proteins, nucleic acid molecules, antibodies and/or inhibitors of the present invention are disclosed herein.

The present invention also includes a therapeutic composition comprising at least one IL-4-, Flt-3 ligand-, CD40-, CD154-, IL-5-, IL-13-, IFN $\alpha$ -, and/or GM-CSF-based compound of the present invention in combination with at least one additional therapeutic compound. Examples of such compounds are disclosed herein.

Therapeutic compositions of the present invention can be administered to any animal susceptible to such therapy, preferably to mammals, and more preferably to dogs,

cats, humans, ferrets, horses, cattle, sheep and/or other pets, economic food animals and/or zoo animals. Preferred animals include dogs, cats, horses and/or humans.

A therapeutic composition of the present invention is administered to an animal in an effective manner such that the composition is capable of regulating an immune response in that animal. Therapeutic compositions of the present invention can be administered to animals prior to onset of a disease (i.e., as a preventative vaccine) and/or can be administered to animals after onset of a disease in order to treat the disease (i.e., as a therapeutic vaccine). Preferred diseases to prevent and/or treat include autoimmune diseases, allergic reactions, infectious diseases, tumor development, inflammatory diseases and/or graft rejection. In one embodiment, a therapeutic composition of the present invention is administered with an antigen to enhance an immune response against that antigen.

Therapeutic compositions of the present invention can be formulated in an excipient that the animal to be treated can tolerate. Examples of such excipients include water, saline, Ringer's solution, dextrose solution, Hank's solution, and/or other aqueous physiologically balanced salt solutions. Nonaqueous vehicles, such as fixed oils, sesame oil, ethyl oleate, or triglycerides may also be used. Other useful formulations include suspensions containing viscosity enhancing agents, such as sodium carboxymethylcellulose, sorbitol, or dextran. Excipients can also contain minor amounts of additives, such as substances that enhance isotonicity and chemical stability. Examples of buffers include phosphate buffer, bicarbonate buffer and/or Tris buffer, while examples of preservatives include thimerosal, o-cresol, formalin and/or benzyl alcohol. Standard formulations can either be liquid injectables or solids which can be

taken up in a suitable liquid as a suspension or solution for injection. Thus, in a non-liquid formulation, the excipient can comprise dextrose, human serum albumin, preservatives, etc., to which sterile water or saline can be added prior to administration.

In one embodiment of the present invention, a therapeutic composition can include an adjuvant. Adjuvants are agents that are capable of enhancing the immune response of an animal to a specific antigen. Suitable adjuvants include, but are not limited to, cytokines, chemokines, and/or compounds that induce the production of cytokines and/or chemokines (e.g., granulocyte macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), macrophage colony stimulating factor (M-CSF), colony stimulating factor (CSF), erythropoietin (EPO), interleukin 2 (IL-2), interleukin-3 (IL-3), interleukin 5 (IL-5), interleukin 6 (IL-6), interleukin 7 (IL-7), interleukin 8 (IL-8), interleukin 10 (IL-10), interleukin 12 (IL-12), interferon gamma, interferon gamma inducing factor I (IGIF), transforming growth factor beta, RANTES (regulated upon activation, normal T cell expressed and presumably secreted), macrophage inflammatory proteins (e.g., MIP-1 alpha and MIP-1 beta), and *Leishmania* elongation initiating factor (LEIF)); bacterial components (e.g., endotoxins, in particular superantigens, exotoxins and cell wall components); aluminum-based salts; calcium-based salts; silica; polynucleotides; toxoids; serum proteins, viral coat proteins; block copolymer adjuvants (e.g., Hunter's Titermax™ adjuvant (Vaxcel™, Inc. Norcross, GA), Ribi adjuvants (Ribi ImmunoChem Research, Inc., Hamilton, MT); and saponins and their derivatives (e.g., Quil A (Superfos Biosector A/S, Denmark). Protein adjuvants of the present invention can be delivered in the form of the protein themselves or of nucleic acid molecules encoding such proteins using the methods described herein.

In one embodiment of the present invention, a therapeutic composition can include a carrier. Carriers include compounds that increase the half-life of a therapeutic composition in the treated animal. Suitable carriers include, but are not limited to, polymeric controlled release vehicles, biodegradable implants, liposomes, bacteria, viruses, other cells, oils, esters, and glycols.

One embodiment of the present invention is a controlled release formulation that is capable of slowly releasing a composition of the present invention into an animal. As used herein, a controlled release formulation comprises a composition of the present invention in a controlled release vehicle. Suitable controlled release vehicles include, but are not limited to, biocompatible polymers, other polymeric matrices, capsules, microcapsules, microparticles, bolus preparations, osmotic pumps, diffusion devices, liposomes, lipospheres, and transdermal delivery systems. Other controlled release formulations of the present invention include liquids that, upon administration to an animal, form a solid or a gel *in situ*. Preferred controlled release formulations are biodegradable (i.e., bioerodible).

A preferred controlled release formulation of the present invention is capable of releasing a composition of the present invention into the blood of the treated animal at a constant rate sufficient to attain therapeutic dose levels of the composition to regulate an immune response in an animal. The therapeutic composition is preferably released over a period of time ranging from about 1 to about 12 months. A controlled release formulation of the present invention is capable of effecting a treatment preferably for at least about 1 month, more preferably for at least about 3 months, even more preferably for

at least about 6 months, even more preferably for at least about 9 months, and even more preferably for at least about 12 months.

Therapeutic compositions of the present invention can be administered to animals prior to and/or after onset of disease. Acceptable protocols to administer therapeutic compositions in an effective manner include individual dose size, number of doses, frequency of dose administration, and/or mode of administration. Determination of such protocols can be accomplished by those skilled in the art. A suitable single dose is a dose that is capable of regulating the immune response in an animal when administered one or more times over a suitable time period. For example, a preferred single dose of a protein, mimotope or antibody therapeutic composition is from about 1 microgram ( $\mu\text{g}$ ) to about 10 milligrams (mg) of the therapeutic composition per kilogram body weight of the animal. Booster vaccinations can be administered from about 2 weeks to several years after the original administration. Booster administrations preferably are administered when the immune response of the animal becomes insufficient to protect the animal from disease. A preferred administration schedule is one in which from about 10  $\mu\text{g}$  to about 1 mg of the therapeutic composition per kg body weight of the animal is administered from about one to about two times over a time period of from about 2 weeks to about 12 months. Modes of administration can include, but are not limited to, subcutaneous, intradermal, intravenous, intranasal, intraocular, oral, transdermal and/or intramuscular routes.

According to one embodiment, a nucleic acid molecule of the present invention can be administered to an animal in a fashion to enable expression of that nucleic acid molecule into a therapeutic protein or therapeutic RNA (e.g., antisense RNA, ribozyme,

triple helix forms or RNA drug) in the animal. Nucleic acid molecules can be delivered to an animal in a variety of methods including, but not limited to, (a) administering a naked (i.e., not packaged in a viral coat or cellular membrane) nucleic acid as a genetic vaccine (e.g., as naked DNA or RNA molecules, such as is taught, for example in Wolff et al., 1990, *Science* 247, 1465-1468) or (b) administering a nucleic acid molecule packaged as a recombinant virus vaccine or as a recombinant cell vaccine (i.e., the nucleic acid molecule is delivered by a viral or cellular vehicle).

A genetic (i.e., naked nucleic acid) vaccine of the present invention includes a nucleic acid molecule of the present invention and preferably includes a recombinant molecule of the present invention that preferably is replication, or otherwise amplification, competent. A genetic vaccine of the present invention can comprise one or more nucleic acid molecules of the present invention in the form of, for example, a dicistronic recombinant molecule. Preferred genetic vaccines include at least a portion of a viral genome (i.e., a viral vector). Preferred viral vectors include those based on alphaviruses, poxviruses, adenoviruses, herpesviruses, picornaviruses, and/or retroviruses, with those based on alphaviruses (such as sindbis or Semliki forest virus), species-specific herpesviruses and/or poxviruses being particularly preferred. Any suitable transcription control sequence can be used, including those disclosed as suitable for protein production. Particularly preferred transcription control sequences include cytomegalovirus immediate early (preferably in conjunction with Intron-A), Rous sarcoma virus long terminal repeat, and tissue-specific transcription control sequences, as well as transcription control sequences endogenous to viral vectors if viral vectors are used. The incorporation of a “strong” polyadenylation signal is also preferred.

Genetic vaccines of the present invention can be administered in a variety of ways, with intramuscular, subcutaneous, intradermal, transdermal, intranasal and/or oral routes of administration being preferred. A preferred single dose of a genetic vaccine ranges from about 1 nanogram (ng) to about 600  $\mu$ g, depending on the route of administration and/or method of delivery, as can be determined by those skilled in the art. Suitable delivery methods include, for example, by injection, as drops, aerosolized and/or topically. Genetic vaccines of the present invention can be contained in an aqueous excipient (e.g., phosphate buffered saline) alone or in a carrier (e.g., lipid-based vehicles).

A recombinant virus vaccine of the present invention includes a recombinant molecule of the present invention that is packaged in a viral coat and that can be expressed in an animal after administration. Preferably, the recombinant molecule is packaging- or replication-deficient and/or encodes an attenuated virus. A number of recombinant viruses can be used, including, but not limited to, those based on alphaviruses, poxviruses, adenoviruses, herpesviruses, picornaviruses, and/or retroviruses. Preferred recombinant virus vaccines are those based on alphaviruses (such as Sindbis virus), raccoon poxviruses, species-specific herpesviruses and/or species-specific poxviruses. An example of methods to produce and use alphavirus recombinant virus vaccines are disclosed in U.S. Patent Number 5,766,602 by Xiong et al., issued June 16, 1998, which is incorporated by this reference herein in its entirety.

When administered to an animal, a recombinant virus vaccine of the present invention infects cells within the immunized animal and directs the production of a therapeutic protein or RNA nucleic acid molecule that is capable of protecting the animal from disease caused by a parasitic helminth as disclosed herein. For example, a



recombinant virus vaccine comprising an immunoregulatory nucleic acid molecule of the present invention is administered according to a protocol that results in the regulation of an immune response in an animal. A preferred single dose of a recombinant virus vaccine of the present invention is from about  $1 \times 10^4$  to about  $1 \times 10^8$  virus plaque forming units (pfu) per kilogram body weight of the animal. Administration protocols are similar to those described herein for protein-based vaccines, with subcutaneous, intramuscular, intranasal, intraocular and/or oral administration routes being preferred.

A recombinant cell vaccine of the present invention includes recombinant cells of the present invention that express at least one protein of the present invention. Preferred recombinant cells for this embodiment include *Salmonella*, *E. coli*, *Listeria*, *Mycobacterium*, *S. frugiperda*, yeast, (including *Saccharomyces cerevisiae* and *Pichia pastoris*), BHK, CV-1, myoblast G8, COS (e.g., COS-7), Vero, MDCK and CRFK recombinant cells. Recombinant cell vaccines of the present invention can be administered in a variety of ways but have the advantage that they can be administered orally, preferably at doses ranging from about  $10^8$  to about  $10^{12}$  cells per kilogram body weight. Administration protocols are similar to those described herein for protein-based vaccines. Recombinant cell vaccines can comprise whole cells, cells stripped of cell walls or cell lysates.

The efficacy of a therapeutic composition of the present invention to regulate the immune response in an animal can be tested in a variety of ways including, but not limited to, detection of cellular immunity within the treated animal, determining lymphocyte or dendritic cell activity, detection of immunoglobulin levels, determining hematopoietic stem cell or hematopoietic early progenitor cell development, determining

dendritic cell development or challenge of the treated animal with an infectious agent to determine whether the treated animal is resistant to disease. In one embodiment, therapeutic compositions can be tested in animal models such as mice. Such techniques are known to those skilled in the art.

5 One embodiment of the present invention is an inhibitory compound. Preferably, such an inhibitory compound is derived from an IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF protein of the present invention. Examples of inhibitory compounds include an antibody of the present invention, that is administered to an animal in an effective manner (i.e., is administered in an amount so as to be present in the

10 animal at a titer that is sufficient, upon interaction of that antibody with a native IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF protein, to decrease the activity of such proteins in an animal, at least temporarily). Oligonucleotide nucleic acid molecules of the present invention can also be administered in an effective manner, thereby reducing expression of either an IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13,

15 IFN $\alpha$ , and/or GM-CSF protein, in order to interfere with the protein activity targeted in accordance with the present invention. Peptides of an IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF protein of the present invention can also be administered in an effective manner, thereby reducing binding of IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF proteins to the appropriate receptor, in

20 order to interfere with the protein activity targeted in accordance with the present invention. An inhibitory compound of an IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF function can be identified using IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF proteins of the present invention, respectively.

One embodiment of the present invention is a method to identify a compound capable of inhibiting IL-4 function. Such a method includes the steps of: (a) contacting (e.g., combining, mixing) an isolated IL-4 protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of the compound, the IL-4 protein binds to IL-4 receptor or stimulates T cells in a T cell proliferation assay, and (b) determining if the putative inhibitory compound inhibits the binding of IL-4 protein to IL-4 receptor or the stimulation of T cells in a T cell proliferation assay. Another embodiment of the present invention is a method to identify a compound capable of inhibiting Flt-3 ligand function. Such a method includes the steps of: (a) contacting an isolated Flt-3 ligand protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of the compound, the Flt-3 ligand protein binds to Flt-3 receptor or stimulates dendritic precursor cells in a proliferation assay, and (b) determining if the putative inhibitory compound inhibits the binding of Flt-3 ligand protein to Flt-3 receptor or the stimulation of dendritic precursor cells in a proliferation assay. Another embodiment of the present invention is a method to identify a compound capable of inhibiting CD40 function. Such a method includes the steps of (a) contacting an isolated CD40 protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of the compound, the CD40 protein binds to a CD40 binding partner (e.g., CD154) and (b) determining if the putative inhibitory compound inhibits the binding of CD40 protein to the CD40 binding partner. A CD40 binding partner is a molecule that selectively binds to CD40 protein. Likewise, a binding partner for any other immunoregulatory protein of the present invention includes molecules that selectively bind to that particular immunoregulatory protein. Another

embodiment of the present invention is a method to identify a compound capable of inhibiting CD154 function. Such a method includes the steps of (a) contacting an isolated CD154 protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of the compound, the CD154 protein binds to a CD154 binding partner (e.g., CD40) and (b) determining if the putative inhibitory compound inhibits the binding of CD154 protein to the CD154 binding partner. Yet another embodiment of the present invention is a method to identify a compound capable of inhibiting IL-5 function. Such a method includes the steps of: (a) contacting an isolated IL-5 protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of the compound, the IL-5 protein binds to IL-5 receptor or stimulates T cells in a T cell proliferation assay, and (b) determining if the putative inhibitory compound inhibits the binding of IL-5 protein to IL-5 receptor or the stimulation of T cells in a T cell proliferation assay. Another embodiment of the present invention is a method to identify a compound capable of inhibiting IL-13 function. Such a method includes the steps of: (a) contacting an isolated IL-13 protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of the compound, the IL-13 protein binds to IL-13 receptor or stimulates T cells in a T cell proliferation assay, and (b) determining if the putative inhibitory compound inhibits the binding of IL-13 protein to IL-13 receptor or the stimulation of T cells in a T cell proliferation assay. Another embodiment of the present invention is a method to identify a compound capable of inhibiting IFN $\alpha$  function. Such a method includes the steps of: (a) contacting an isolated IFN $\alpha$  protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of the compound, the IFN $\alpha$  protein

binds to IFN $\alpha$  receptor or inhibits proliferation of GM-CSF stimulated TF-1 cells, and (b) determining if the putative inhibitory compound inhibits the binding of IFN $\alpha$  protein to IFN $\alpha$  receptor or inhibits proliferation of GM-CSF stimulated TF-1 cells. Another embodiment of the present invention is a method to identify a compound capable of inhibiting GM-CSF function. Such a method includes the steps of: (a) contacting an isolated GM-CSF protein of the present invention, with a putative inhibitory compound under conditions in which, in the absence of said compound, the GM-CSF protein binds to GM-CSF receptor or stimulates T cells in a T cell proliferation assay, and (b) determining if the putative inhibitory compound inhibits the binding of GM-CSF protein to GM-CSF receptor or the stimulation of T cells in a T cell proliferation assay.

Putative inhibitory compounds to screen include small organic molecules, antibodies (including mimetopes thereof), and/or ligand analogs. Such compounds are also screened to identify those that are substantially not toxic in host animals.

Preferred IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF, proteins to inhibit are those produced by dogs, cats, horses or humans, even more preferred IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF proteins to inhibit are those produced by domestic dogs or cats. A particularly preferred inhibitor of the present invention is capable of regulating an immune response in an animal. It is also within the scope of the present invention to use inhibitors of the present invention to target diseases involving undesired immune activity in animals. Compositions comprising inhibitors of IL-4, Flt-3 ligand, CD40, CD154, IL-5, IL-13, IFN $\alpha$ , and/or GM-CSF function can be administered to animals in an effective manner to regulate the immune response in the animals, and preferably to prevent autoimmune disease, allergy,

infectious disease, inflammation or prevent graft rejection in animals, or to treat animals with such diseases. Effective amounts and/or dosing regimens can be determined using techniques known to those skilled in the art.

It is also within the scope of the present invention to use isolated proteins,  
5 mimetopes, nucleic acid molecules and/or antibodies of the present invention as diagnostic reagents. Methods to use such diagnostic reagents are well known to those skilled in the art, see, for example, Janeway, et al., *ibid.*, and/or PCT Publication No. WO 98/23964, published June 4, 1998.

The following examples are provided for the purposes of illustration and are not  
10 intended to limit the scope of the present invention.

### EXAMPLES

It is to be noted that the examples include a number of molecular biology, microbiology, immunology and biochemistry techniques considered to be familiar to those skilled in the art. Disclosure of such techniques can be found, for example, in  
15 Sambrook et al., *ibid.* and Ausubel, et al., 1993, *Current Protocols in Molecular Biology*, Greene/Wiley Interscience, New York, NY, and related references. Ausubel, et al, *ibid.* is incorporated by reference herein in its entirety.

#### Example 1

This example describes the isolation and sequencing of canine interleukin-4 (IL-4)  
20 nucleic acid molecules of the present invention. This example also describes expression of recombinant canine IL-4 in *E. coli* and mammalian cells; development of monoclonal and polyclonal antibodies to *E. coli* expressed canine IL-4; and bioactivity of mammalian-expressed and *E. coli*-expressed canine IL-4.

A. Isolation and sequencing of a canine IL-4 nucleic acid molecule.

Initial attempts to isolate a canine IL-4 nucleic acid molecule using various primers corresponding to putative conserved regions of IL-4 nucleic acid molecules failed. Forward and reverse primers were then designed using a sequence tag site (IL-4sts) described by Venta et al. in GenBank. The forward primer was designated as IL-4stsA, having the nucleic acid sequence 5' CTATTAATGG GTCTCACCTC CCAA CT 3', designated herein as SEQ ID NO:11. The reverse primer was designated as prIL-4stsB, having the nucleic acid sequence 5' TCAACTCGGT GCACAGAGTC TTGG 3', designated herein as SEQ ID NO:12. The primers were used to amplify PCR products from a *C. familiaris* mitogen activated PBMC cDNA library that was constructed in the Uni-ZAP® XR vector (available from Stratagene Cloning Systems, La Jolla, CA), using Stratagene's ZAP-cDNA® Synthesis Kit and the manufacturer's protocol. The mRNA was isolated from *C. familiaris* peripheral blood mononuclear cells about 4 hours after they were activated by a polyclonal activating agent in culture. Four PCR products were produced that had the expected size range. The PCR products were cloned and sequenced using standard techniques. A portion of one of the four products was found to be somewhat homologous with an IL-4 nucleic acid sequence reported in GenBank.

To identify a cDNA encoding a full-length canine IL-4 protein, the PCR product showing some homology with the IL-4 sequence reported in GenBank was used to generate an about 549 base pair DNA fragment as follows. The PCR product was labeled with <sup>32</sup>P and used as a probe to screen the canine PBMC cDNA library. Hybridization was done at about 6X SSC, 5X Denhardt's solution, 0.5 % SDS, 100 µg/ml of ssDNA and



100  $\mu$ g/ml of tRNA, at about 68°C, for about 36 hr. (the compositions of SSC and Denhardt's are described in Sambrook et al., *ibid.*). The filters were washed 3 times, for about 30 minutes per wash, at about 55° C in about 2X SSC, 0.2% SDS, followed by a final wash of about 30 minutes in the same buffer except using about 1X SSC. Positive clones were isolated and the cDNA inserts were sequenced for both strands using vector flanking primers and gene-specific internal primers. Sequence analysis was performed using the GAP program of GCG (available from the University of Wisconsin) using the alignment settings of: gap weight set at 50, length weight set at 3, and average match set at 10 for nucleic acid sequence comparisons; and gap weight set at 12, length weight set at 4, and average match set at 2.912 for amino acid sequence comparisons.

A cDNA nucleic acid molecule was isolated, referred to herein as nCaIL-4<sub>549</sub>, the coding strand of which was shown to have a nucleic acid sequence denoted herein as SEQ ID NO:1. The complement of SEQ ID NO:1 is represented herein by SEQ ID NO:3. Translation of SEQ ID NO:1 suggests that nucleic acid molecule nCaIL-4<sub>549</sub> encodes a full-length IL-4 protein of about 132 amino acids, denoted herein as PCaIL-4<sub>132</sub>, the amino acid sequence of which is presented in SEQ ID NO:2, assuming an open reading frame having an initiation codon spanning from nucleotide 43 through nucleotide 45 of SEQ ID NO:1 and a stop codon spanning from nucleotide 439 through nucleotide 441 of SEQ ID NO:1. The coding region encoding PCaIL-4<sub>132</sub> is presented herein as nCaIL-4<sub>396</sub>, which has the nucleotide sequence SEQ ID NO:4 (the coding strand) and SEQ ID NO:5 (the complementary strand). A putative signal sequence coding region extends from nucleotide 43 through nucleotide 114 of SEQ ID NO:1. The proposed mature protein (i.e., canine IL-4 protein from which the signal sequence has been cleaved), denoted

herein as PCaIL-4<sub>108</sub>, contains about 108 amino acids, extending from residue 25 through residue 132 of SEQ ID NO:2; PCaIL-4<sub>108</sub> amino acid sequence is represented herein as SEQ ID NO:20. The nucleic acid molecule encoding PCaIL-4<sub>108</sub> is denoted herein as nCaIL-4<sub>324</sub>, extending from nucleotide 115 through nucleotide 438 of SEQ ID NO:1.

- 5 nCaIL-4<sub>324</sub> has a coding sequence denoted SEQ ID NO:19 and a complementary sequence denoted SEQ ID NO:21.

Comparison of nucleic acid sequence SEQ ID NO:1 with nucleic acid sequences reported in GenBank indicates that SEQ ID NO:1 showed the most homology, i.e., about 89.3% identity, with a feline IL-4 gene. Comparison of amino acid sequence SEQ ID  
10 NO:2 with amino acid sequences reported in GenBank indicates that SEQ ID NO:2 showed the most homology, i.e., about 82.6% identity, with a feline IL-4 protein. Sequence analysis was performed using the GCG GAP program as described above.

B. Expression of recombinant canine IL-4 in *E. coli* and mammalian cells

i. *E. coli* expression

- 15 A recombinant molecule capable of expressing the mature form of canine IL-4, denoted herein as pGEX-nCaIL-4<sub>327</sub>, was produced as follows. A 340-nucleotide fragment was PCR amplified from nucleic acid molecule nCaIL-4<sub>549</sub> (having coding strand SEQ ID NO:1) using the following primer sequences: positive strand 5'  
TGAATTCGGA CATAACTTCA ATATTAC 3' (SEQ ID NO:38) (*Eco*RI site in bold)  
20 and 5' TCTCGAGATT CAGCTTCATG CCTGTA 3' (SEQ ID NO:39) (*Xho*I site in bold). The resulting 340-base pair fragment was digested with *Eco*RI and *Xho*I restriction enzymes (available from New England Biolabs, Beverly, MA), according to the

manufacturer's directions, and gel-purified using standard techniques. The digested 340-base pair fragment, now 327 base pairs, was then ligated into pGEX-6P-1 (available from Amersham Pharmacia, Piscataway, NJ), which had been previously digested with *EcoRI* and *XhoI* and gel purified, to produce recombinant molecule pGEX-nCaIL-4<sub>327</sub>.

- 5 Recombinant molecules of pGEX produce the protein of interest as a glutathione s-transferase (GST) fusion protein. The recombinant molecule pGEX-nCaIL-4<sub>327</sub> was transformed into DH5alpha cells (available from Life Technologies, Gaithersburg, MD), a recombination deficient strain of *E. coli*, to produce recombinant cell DH5-pGEX-nCaIL-4<sub>327</sub>. The recombinant cells were screened for presence of insert by PCR and
- 10 confirmed by enzyme restriction analysis and nucleic acid sequencing, using standard techniques. Several clonal recombinant molecules were transformed into BL21 cells (available from Amersham Pharmacia, Piscataway, NJ), a protease deficient strain of *E. coli*, to produce recombinant cell BL21-pGEX-nCaIL-4<sub>327</sub>. These recombinant cells were screened, and the clone with the highest level of protein yield was selected for scaling up
- 15 for larger-scale protein production. The resultant recombinant protein is referred to herein as *E. coli*PCaIL-4<sub>109</sub>.

- To produce and purify *E. coli*PCaIL-4<sub>109</sub>, bacterial cultures of recombinant cell BL21:pGEX-nCaIL-4<sub>327</sub> were grown in shake flasks at 37°C and induced with 0.1 mM IPTG (isopropyl-β-D-thiogalactopyranoside), (available from Sigma Chemical Company,
- 20 St. Louis, MO) when OD<sub>600nm</sub> reached about 0.8 units. Growth was allowed to continue for about 4 hours; then bacteria were harvested by centrifugation at 4000 x g (times gravity) for 20 minutes. The bacterial pellet was washed and resuspended in phosphate buffered saline (PBS) (for recipe, see Sambrook et al, *ibid.*), then lysed by exposure to

gaseous nitrogen pressure in a Parr pressure vessel (available from Parr Instrument Co., Moline, IL), according to the manufacturer's instructions. Cell debris was removed by centrifugation at 10,000 x g for 20 minutes. The IL-4-GST fusion protein *E. coli*PCaIL-4<sub>109</sub> was purified from the supernatant by allowing incubation with glutathione-  
 5 conjugated resin, removing unbound proteins and then removing the GST tag with PRESCISSION™ protease; all reagents were available from Amersham Pharmacia and all were used according to the manufacturer's directions.

Concentration and purity of *E. coli*PCaIL-4<sub>109</sub> were estimated by BCA Protein Assay kit (available from Pierce, Rockford, IL) and SDS-PAGE followed by Coomassie  
 10 staining, respectively. The purified material exhibited a single band of approximately 14 kilodaltons (kD) by Coomassie stained SDS-PAGE.

ii. CHO cell expression

A recombinant molecule denoted herein as pCMV-nCaIL-4<sub>399</sub>, capable of expressing a full length form of canine IL-4 (including signal sequence) was produced as  
 15 follows. A 422-nucleotide fragment was PCR amplified from nucleic acid molecule nCaIL-4<sub>549</sub> using the following primers: 5' **CCCAAGCTTA** TGGGTCTCACC TCCCAAC (*Hind*III site in bold), denoted SEQ ID NO:40, and 3' CCTCGAGATT CAGCTTTCAA TGCCTGTA (*Xho*I site in bold), denoted SEQ ID NO:127. The 422-  
 base pair PCR product was digested with the restriction endonucleases *Hind*III and *Xho*I,  
 20 both available from New England Biolabs. The resulting 399-base pair product encoding full-length canine IL-4 was gel purified using standard techniques and ligated into the cytomegalovirus (CMV) immediate-early transcription control region of the pCMV-Int A

plasmid vector that had been digested with *HindIII* and *XhoI* (available from New England Biolabs), and gel purified, to produce the recombinant molecule pCMV-nCaIL-4<sub>399</sub>. The pCMV-Int A plasmid vector was generated as referenced by J.E. Osorio et al., 1999, *Vaccine* 17, 1109-1116. Briefly, vector pRc/RSV, (available from Invitrogen Corp., San Diego, CA) was cleaved with restriction enzyme *PvuII* (available from New England Biolabs), and the 2963-base pair *PvuII* fragment was gel purified. The fragment was self-ligated to form the vector pRc/RSV(*Pvu*), which contains a Rous Sarcoma Virus (RSV) long terminal repeat, a multiple cloning site, a bovine growth hormone polyadenylation sequence, a bacterial origin of replication, and an ampicillin resistance gene. Vector pRc/RSV(*Pvu*) was restriction enzyme digested using *HindIII* and *NruI*. A *HindIII/SspI* fragment containing the HCMV intermediate early promoter and first intron (i.e. intron A) was ligated into the digested pRc/RSV(*Pvu*) vector to produce the vector pCMV-Int A.

Stable expression of CaIL-4 in mammalian cells was carried out by transfecting the recombinant molecule pCMV-nCaIL-4<sub>399</sub> into Chinese Hamster Ovary cells, (CHO, available from ATCC) as follows. Six-well polystyrene tissue culture plates (available from Corning Costar, Acton, MA) were seeded with approximately  $5 \times 10^5$  cells/well in 2 milliliter (ml) cell culture media, consisting of Minimal Essential Media (MEM) supplemented with 100 mM L-glutamine, 100 mM gentamicin, and 10% fetal bovine serum (FBS), (all available from Life Technologies). Cells were grown to about 80% confluence (for about 18 hours) before transfection. The recombinant molecules to be transfected were purified using the Plasmid Midi Kit (available from Qiagen, Valencia, CA) and used according to the manufacturer's instructions. The recombinant molecule

pCMV-nCaIL-4<sub>399</sub> was linearized using the restriction enzyme *PvuI* (available from New England Biolabs). The plasmid pcDNA3, (available from Invitrogen), which contains the neomycin resistance gene, was linearized using the restriction enzyme *EcoRI*.

Approximately 2  $\mu$ g of pCMV-nCaIL-4<sub>399</sub> was mixed with about 2 ng of linearized  
 5 pcDNA3 in about 100  $\mu$ l OPTIMEM™ media, available from Life Technologies. About 10  $\mu$ l Lipofectamine, (available from Life Technologies) was mixed with 100  $\mu$ l OPTIMEM. The nucleic acid molecule-containing mixture was then added to the Lipofectamine mixture and incubated at room temperature for about 45 minutes. After incubation, about 0.8 ml OPTIMEM was added, and the mixture was overlaid onto the  
 10 CHO cells which had been previously rinsed with OPTIMEM. Cells were incubated for about 5 hours at 37°C 5% CO<sub>2</sub>, 95% relative humidity. Approximately 1 ml of cell culture media as described previously, with 20% FBS, was added and the cells were incubated overnight. The media was changed at 24 hours, and at 72 hours post transfection, the cells were split 1:4 and put into fresh cell culture media containing about  
 15 500  $\mu$ g/ml geneticin (G418, available from Life Technologies). The media was changed every 3-5 days. After several weeks, G418 resistant colonies were trypsinized using sterile filter papers, 5-6 mm in diameter that were soaked in trypsin, which were then placed over individual wells of 24 well plates that contained separated widely spaced colonies of CHO cells. After 3 days, the papers were removed. The resulting  
 20 recombinant cells are referred to herein as CHO-pCMV-nCaIL-4<sub>399</sub>. The recombinant cells were then expanded and tested for the presence of nIL-4<sub>399</sub> RNA by RT-PCR and tested for the presence of PCaIL-4<sub>133</sub> protein by Western blot analysis. Westerns were developed with rabbit anti-*E. coli*PCaIL-4<sub>109</sub> serum and 607.1 monoclonal antibody, a

monoclonal antibody that selectively binds to *E. coli*PCaIL-4<sub>109</sub> protein. See Example 1C for a description of how these antibodies were produced.

C. Monoclonal and polyclonal antibodies to recombinant canine IL-4 (i.e., anti-canine IL-4 antibodies)

5 The following describes the development of monoclonal and polyclonal antibodies that selectively bind to *E. coli*PCaIL-4<sub>109</sub>.

Female Balb/C mice, 6-8 weeks old, were injected subcutaneously, at about 4 sites, with a total of 25 $\mu$ g *E. coli*PCaIL-4<sub>109</sub> (produced as described in Example 1Bi) in Freund's Complete Adjuvant (day 0). Fourteen days later, the mice received an

10 intraperitoneal boost of 25 $\mu$ g *E. coli*PCaIL-4<sub>109</sub> in Freund's Incomplete Adjuvant (day 14). Fourteen days later, serum was tested for antibody titer to *E. coli*PCaIL-4<sub>109</sub> by ELISA (day 28). Three days prior to fusion, mice were boosted intravenously with 20 $\mu$ g *E. coli*PCaIL-4<sub>109</sub> in PBS (day 35). Splenocytes were harvested from mice demonstrating the highest serum titer by ELISA and depleted of CD4+ and CD8+ cells. This depletion

15 was achieved by incubation of the splenocytes with biotinylated rat anti-mouse CD4 and anti-mouse CD8 monoclonal antibodies, available from PharMingen, San Diego, CA. Antibody-labeled cells were then removed by incubation with M-280 streptavidin coated magnetic beads, available from Dynal, Oslo, Norway. Depleted splenocytes were fused to SP2/0 cells (available from ATCC) using 50% polyethylene glycol in unsupplemented

20 Iscove's Modified Dulbecco's Media (IMDM), following established protocols; see, for example, Harlow E., and Lane D., eds., 1995, *Antibodies. A Laboratory Manual*, Monoclonal Antibodies, Cold Spring Harbor Laboratories; Harlow et al, *ibid.*, is incorporated by reference herein in its entirety. Fused cells were plated in 96-well plates



using IMDM cell culture media, (available from Life Technologies, Inc., Rockville, MD), which was supplemented with 10% fetal bovine serum, 2 mM L-glutamine, 1 mM sodium pyruvate, 1 X nonessential amino acids, 1 X MEM amino acids, 0.05 mg/ml gentamicin, and 0.5 mM  $\beta$ -mercaptoethanol (all reagents available from Life Technologies). Additionally, 100  $\mu$ M hypoxanthine, 0.4  $\mu$ M aminopterin, and 16  $\mu$ M thymidine, all available from Sigma Chemical Corporation, St Louis, MO, were added.

After about 7 days, wells positive for hybridoma growth were screened by ELISA to *E. coli*PCaIL-4<sub>109</sub>. Immulon II 96-well plates (available from VWR, Denver, CO) were coated, overnight, with 100 ng/ml *E. coli*PCaIL-4<sub>109</sub> in 0.1 M carbonate/bicarbonate buffer, Ph 9.6. After blocking the wells with 20% FBS in Tris buffered saline (TBS), culture supernatants were allowed to bind. Presence of anti-*E. coli*PCaIL-4<sub>109</sub> mouse antibody was detected with polyclonal goat anti-mouse IgG conjugated to horseradish peroxidase, (available from KPL, Gaithersburg, MD), and color developed with 3,3',5,5'-tetramethylbenzidine dihydrochloride (TMB), available from Pierce, Rockford, IL. Specificity of the ELISA reactivity was verified by Western blot analysis to *E. coli*PCaIL-4<sub>109</sub>, developed with polyclonal goat anti-mouse IgG conjugated to alkaline phosphatase and nitro-blue tetrazolium/5-bromo-4-chloro-3'-indolyphosphate p-toluidine salt substrate (NBT/BCIP, available from Sigma). Western blots exhibited a single band of approximately 14 kD. Immunoglobulin isotype of the monoclonal antibodies was determined using IsoStrips, available from Boehringer Mannheim, Indianapolis, IN. Twenty-three monoclonal antibodies were generated to *E. coli*PCaIL-4<sub>109</sub>, 22 of which were of the IgM isotype and one of which was IgG1, and is referred to herein as 607.1.

Polyclonal rabbit serum was produced by repeated immunization (over a 10 month period) of a male, New Zealand White rabbit 12-16 months old. Initial immunization was 50 ug *E. coli*PCaIL-4<sub>109</sub> (prepared as described in Example 1bi) in Freund's Complete Adjuvant, at several sites subcutaneously and intradermally. One month later, and at one month intervals thereafter, the rabbit was boosted intradermally with 50 ug *E. coli*PCaIL-4<sub>109</sub> in Freund's Incomplete Adjuvant. Serum was collected bi-weekly and titers monitored by ELISA and Western blot to *E. coli*PCaIL-4<sub>109</sub>. Serum that selectively bound to *E. coli*PCaIL-4<sub>109</sub> protein is referred to as anti-*E. coli*PCaIL-4<sub>109</sub> serum.

#### 10 D. Bioactivity of mammalian-expressed canine IL-4

The following describes a bioassay to detect the expression of canine IL-4 protein expressed in the supernatants from CHO-pCMV-nCaIL-4<sub>399</sub> recombinant cells by screening for production of CD23.

About 100  $\mu$ l Ramos cells, available from ATCC, at a concentration of about 3.5 x 10<sup>3</sup> cells/ ml were seeded into 96-well flat bottom plates, available from Becton Dickinson, Franklin Lakes, NJ). These cells were grown in RPMI media supplemented with 100 mM L-glutamine, gentamicin, and 10 % FBS (called TCM). The Ramos cells were then treated in 5% CO<sub>2</sub> for 37°C for approximately 48 h. with one of the following:

Group	Treatment
20 1	TCM
2	CHO-pCMV (a transfectant cell line containing the empty pCMV vector) supernatant (1:4 final dilution in TCM)
3	CHO-pCMV-nCaIL-4 <sub>399</sub> supernatant (1:20 final dilution in TCM)

Triplicate samples for each treatment group were pooled for staining to look for increased expression of CD23 (one of the reported effects of IL-4). Briefly,  $1 \times 10^5$  cells from each treatment group were incubated in phosphate buffered saline (PBS) containing 30% FBS for 15-30 min on ice. The cells were collected and incubated with the

5 following:

<u>Condition</u>	<u>Primary Incubation</u>	<u>Secondary Incubation</u>
A	PBS	Goat anti mouse PE
B	Mouse anti human CD23	Goat anti mouse PE

10 Mouse anti-human CD23 monoclonal antibody, available from Pharmingen, was used at about  $10 \mu\text{g/ml}$ . Goat (Fab'2) anti mouse IgG PE, available from Southern Biotechnologies was used at about  $2.5 \mu\text{g/ml}$ . These reagents were diluted in PBS with 5% FBS. Primary incubations were performed for 30-60 minutes on ice, and secondary incubations were performed for 20-30 min on ice. Three washes of PBS/5% FBS were performed in between each incubation. Cells were then analyzed on a flow cytometer

15 (e.g., MoFlow Desk Top System, available from Cytomation, Ft. Collins, CO) with the fluorescein gate set at  $10^1$ . The results are shown in Table 2.

Table 2. Induction of CD23 on Ramos cells post-treatment with supernatants from CHO-pCMV-nCaIL-4<sub>399</sub>

Treatment	Condition	% positive
1	A	0
	B	1
2	A	8
	B	1
3	A	3
	B	99

Table 2 shows that the canine IL-4 expressed by the CHO transfectant CHO-pCMV-nCaIL-4<sub>399</sub> is biologically active, demonstrated by its ability to induce expression of CD23 in Ramos cells.

E. Bioactivity of *E. coli*-expressed canine IL-4

5 The following describes a bioassay to detect the expression of canine IL-4 by stimulating the proliferation of TF-1 cells.

TF-1 cells (a human erythroleukaemia cell line, available from R&D Systems, Minneapolis, MN), were grown and maintained in TCM-TF-1 medium (RPMI-1640 media supplemented with 2 mM L-glutamine, 5 µg/ml gentamicin, 5% FBS and 2 ng/ml  
10 recombinant human GM-CSF (rhuGM-CSF, available from R&D Systems)) in 5% CO<sub>2</sub> at 37°C

For assay, TF-1 cells were extensively washed to remove rhuGM-CSF, then added at approximately 1 x 10<sup>4</sup> cells per well to 96-well flat bottom plates. Refolded and HPLC-purified *E. coli*-expressed PCaIL-4<sub>109</sub>, produced as described in Example 1Bi, was  
15 diluted to the appropriate concentration in TCM-TF-1 without rhuGM-CSF and filter sterilized. Cells and *E. coli*-expressed PCaIL-4<sub>109</sub> were incubated for 48 hours in 5% CO<sub>2</sub> at 37°C, then pulsed with 1 µCi/well tritiated thymidine (available from ICN Pharmaceuticals, Irvine, CA), and incubated for an additional 18 hours. Contents of the wells were harvested onto glass fiber filters and counted in a Wallac Trilux 1450  
20 scintillation counter (available from Wallac Inc., Gaithersburg, MD). The results are shown in Table 3.

Table 3. Stimulation of proliferation of TF-1 cells with *E. coli*-expressed PCaIL-4<sub>109</sub>

	<u>Concentration <i>E. coli</i> PcaIL-4<sub>109</sub></u> <u>(ng/ml)</u>	<u>Counts per minute</u>
5	1000	33,216
	500	26,297
	250	27,283
	125	23,804
	62.5	26,225
10	31.3	19,803
	15.6	9,818
	7.8	6,475
	0	165

Table 3 shows that canine IL-4 expressed by *E. coli* is biologically active, as demonstrated by its ability to stimulate proliferation of TF-1 cells.

## 15 Example 2

This example describes the isolation and sequencing of certain canine Flt-3 ligand and feline Flt-3 nucleic acid molecules and proteins of the present invention. The example also describes expression of a canine Flt-3 ligand protein of the present invention in CHO cells, as well as detection of the expressed canine Flt-3 ligand protein.

### 20 A. Canine Flt-3 ligand nucleic acid molecules and proteins.

i. This example describes the isolation and sequencing of certain canine Flt-3 ligand nucleic acid molecules and proteins of the present invention.

A canine Flt-3 ligand nucleic acid molecule was produced as follows. A pair of primers was initially used to amplify DNA from the *C. familiaris* mitogen activated  
 25 PBMC cDNA library described above in Example 1. A forward primer referred to as FLT3F1, having the nucleic acid sequence 5' CTGGCGCCAG CCTGGAGCCC 3', designated herein as SEQ ID NO:13 was used in combination with a reverse primer

referred to herein as FLT3B1, having the nucleic acid sequence 5' GGGAGATGTT  
GGTCTGGACG 3', referred to herein as SEQ ID NO:14 to amplify Flt-3 ligand DNA  
from the cDNA library by polymerase chain reaction (PCR). The primers were designed  
using conserved regions of IL-4 cDNA sequences from other species in the public  
5 databases corresponding to the positions shown below:

	Database	Accession number	Nucleotides	Animal
	gb	U04806	102-121	human
	gb	L23636	41-60	mouse
10	gb	U04806	77-458	human
	gb	L23636	419-400	mouse

A 360-base pair (bp) PCR product was generated in the above reaction that was  
purified, radiolabeled and used as a probe to screen the cDNA library. Hybridization was  
performed in 6X SSC, 5X Denhardt's solution, 0.5 % SDS, 100  $\mu$ g/ml ssDNA and 100  
15  $\mu$ g/ml of tRNA, at 68°C, for about 36 hr. The filters were washed 3 times, for about 30  
minutes per wash, at 55°C in 2X SSC, 0.1% SDS, followed by a final wash in 0.25X  
SSC, for about 30 minutes, at 55° C. Several positive phage clones were identified and  
shown to produce PCR products when used as templates in combination with the FLT3F1  
and FLT3B1 primers. The DNA inserts in the phage clones were sequenced using  
20 standard techniques and failed to yield any clones containing DNA inserts having a  
portion homologous to published Flt-3 ligand sequences. The 360-bp PCR fragment  
generated above was then cloned into the vector pcDNA 2.1 (available from Invitrogen  
Corp., San Diego, CA). Several independent colonies were generated and the sequences  
of their inserts determined. One clone was identified that which contained insert

sequence having a portion that was somewhat homologous to published human or murine Flt-3 ligand sequence.

Two canine Flt-3 ligand-specific primers were then designed using the nucleic acid sequence obtained using the 360-bp PCR product described above.

5	<u>Primer</u>	<u>Sequence</u>	<u>SEQ ID NO</u>
	DFLB1	5' GACCAGGCGCCAGAACGC 3'	SEQ ID NO:15
	DFLF1	5' CGGTCACCATCCGCAAGC 3'	SEQ ID NO:16

The 5' region of a Flt-3 ligand nucleic acid molecule was PCR amplified from the cDNA library using the DFLB1 primer in combination with the 5' T3 vector primer from the Uni-ZAP® XR vector (available from Stratagene). The 3' region of a Flt-3 ligand nucleic acid molecule was PCR amplified from the cDNA library using the DFLF1 in combination with the 3' T7 primer from the Uni-ZAP® XR vector (available from Stratagene). A 855-bp PCR product was obtained representing the 5' region of a Flt-3 ligand nucleic acid molecule. A 265-bp PCR product was obtained representing the 3' region of a Flt-3 ligand nucleic acid molecule. Both the 855-bp PCR product and 265-bp PCR product were cloned and sequenced using standard methods. Additional canine Flt-3 ligand-specific primers were designed using the nucleic acid sequence obtained from the sequence of the 855-bp PCR product and 265-bp PCR products.

	<u>Primer</u>	<u>Sequence</u>	<u>SEQ ID NO</u>
20	DFLB2	5' TGGCAAGGCAGTGGCCTC 3'	SEQ ID NO:17
	DFLF2	5' GCCGAGATGATAGTGCTGGC 3'	SEQ ID NO:18

A 546-bp PCR product was generated using the primer DFLF2 in combination with the primer DFLB2 to amplify a PCR product from the cDNA library. The 546-bp



PCR product was then purified, radiolabelled and used as a probe to screen the cDNA library. Hybridization was performed in 6X SSC, 5X Denhardt's solution, 0.5 % SDS, 100  $\mu$ g/ml of ssDNA and 100  $\mu$ g/ml of tRNA, at 68°C, for about 36 hr. The filters were washed in 1.25X SSC, for about 30 minutes, at 55°C. Four cDNA clones encoding

5 full-length canine Flt-3 ligand were isolated. Nucleic acid sequence was obtained using standard techniques.

A Flt-3 ligand clone was isolated, referred to herein as nCaFlt3L<sub>1013</sub>, the coding strand of which was shown to have a nucleic acid sequence denoted herein as SEQ ID NO:6. The complement of SEQ ID NO:6 is represented herein by SEQ ID NO:8.

10 Translation of SEQ ID NO:6 suggests that nucleic acid molecule nCaFlt3L<sub>1013</sub> encodes a full-length Flt-3 ligand protein of about 294 amino acids, denoted herein as PCaFlt3L<sub>294</sub>, the amino acid sequence of which is presented in SEQ ID NO:7, assuming an open reading frame having an initiation codon spanning from nucleotide 35 through nucleotide 37 of SEQ ID NO:6 and a stop codon spanning from nucleotide 917 through nucleotide

15 919 of SEQ ID NO:6. The coding region encoding PCaFlt3L<sub>294</sub> is presented herein as nCaFlt3L<sub>882</sub>, which has the nucleotide sequence SEQ ID NO:9 (the coding strand) and SEQ ID NO:10 (the complementary strand). A putative signal sequence coding region extends from nucleotide 35 through nucleotide 112 of SEQ ID NO:6. The proposed mature protein (i.e., canine Flt-3 ligand protein from which the signal sequence has been

20 cleaved), denoted herein as PCaFlt3L<sub>268</sub> (SEQ ID NO:23), contains about 268 amino acids, extending from residue 27 through residue 294 of SEQ ID NO:7. The nucleic acid molecule encoding PCaFlt3L<sub>268</sub> is denoted herein as nCaFlt3L<sub>804</sub>, extending from nucleotide 113 through nucleotide 916 of SEQ ID NO:6. nCaFlt3L<sub>804</sub> has a coding

sequence denoted SEQ ID NO:22 and a complementary sequence denoted SEQ ID NO:24.

Below is a description of the identification of alternatively spliced *Canis* Flt3 ligand transcripts. Besides cDNA clones such as nucleic acid molecule nCaFlt3L<sub>1013</sub> encoding the full-length canine Flt3 ligand protein, two splice variants of canine Flt3 ligand cDNA clones were also isolated, using the same hybridization conditions as mentioned previously in this Example. One such variant (Clone 1), denoted herein as nCaFlt3L<sub>985</sub>, has a coding strand the nucleic acid sequence of which is represented as SEQ ID NO:25. The complement of SEQ ID NO:25 is represented herein by SEQ ID NO:27. Translation of SEQ ID NO:25 suggests that nucleic acid molecule nCaFlt3L<sub>985</sub> encodes a Flt-3 ligand protein of 276 amino acids, denoted herein as PCaFlt3L<sub>276</sub>, the amino acid sequence of which is represented by SEQ ID NO:26, assuming an open reading frame having an initiation codon spanning from nucleotide 74 through nucleotide 76 of SEQ ID NO:25 and a stop codon spanning from nucleotide 902 through nucleotide 904 of SEQ ID NO:25. The coding region encoding PCaFlt3L<sub>276</sub> is represented herein as nCaFlt3L<sub>828</sub>, which has the nucleotide sequence SEQ ID NO:28 (the coding strand) and SEQ ID NO:29 (the complementary strand). Alignment of nucleic acid molecules nCaFlt3L<sub>882</sub> and nCaFlt3L<sub>828</sub> indicates that the nucleic acid molecules are identical except for a deletion in nCaFlt3L<sub>828</sub>, which spans from nucleotide 343 through nucleotide 396 of nCaFlt3L<sub>882</sub>. Accordingly, nCaFlt3L<sub>828</sub> encodes 18 fewer amino acids than nCaFlt3L<sub>882</sub>. The deletion in PCaFlt3L<sub>276</sub>, which spans from residue 115 through residue 132 of PCaFlt3L<sub>294</sub>, occurs between helix III and helix IV of the canine Flt3 ligand protein inferred from alignment with the human and mouse Flt3 ligand protein (Lyman et al.,

*Cell*, vol. 75, pp. 1157-1167, 1993; Hannum et al., *Nature*, vol. 368, pp. 643-648, 1994; Lyamn et al., *Blood*, vol. 83, pp. 2795-2801, 1994). In addition, the alignment shows that there are 39 more nucleotides in the 5' untranslated region of nucleic acid molecule nCaFlt3L<sub>985</sub> (nucleotides 1 to 39) than nucleic acid molecule nCaFlt3L<sub>1013</sub> and there are 2  
5 more nucleotides in the 3' untranslated region of nucleic acid molecule nCaFlt3L<sub>985</sub> (nucleotides 922 to 923) than nucleic acid molecule nCaFlt3L<sub>1013</sub>. The remaining sequences between nCaFlt3L<sub>985</sub> and nCaFlt3L<sub>1013</sub> are identical. A putative mature form of nCaFlt3L<sub>985</sub> (without the signal sequence) is predicted. The putative signal sequence coding region extends from nucleotide 74 to nucleotide 151 of SEQ ID NO:25. The  
10 proposed mature protein, denoted herein as PCaFlt3L<sub>250</sub>, represented by SEQ ID NO:31, contains about 250 amino acids, extending from residue 27 through residue 276 of SEQ ID NO:26. The nucleic acid molecule encoding PCaFlt3L<sub>250</sub>, extending from nucleotide 152 through nucleotide 901 of SEQ ID NO:6, denoted herein as nCaFlt3L<sub>750</sub>, is represented by SEQ ID NO:30 ( the coding strand) and SEQ ID NO:32 (the complement  
15 strand).

A second variant (Clone 19) is represented by nucleic acid molecule nCaFlt3L<sub>1019</sub>, the coding strand of which is denoted herein as SEQ ID NO:33. The complement of SEQ ID NO:33 is denoted herein as SEQ ID NO:35. Translation of SEQ ID NO:33 suggests that nCaFlt3L<sub>1019</sub> encodes a Flt-3 ligand protein of 31 amino acids, PCaFlt3L<sub>31</sub>, denoted  
20 SEQ ID NO:34, assuming an initiation codon spanning from nucleotide 74 through nucleotide 76 and a stop codon spanning nucleotide 167 through nucleotide 169 of SEQ ID NO:33. The coding region encoding PCaFlt3L<sub>31</sub> is represented herein as nCaFlt3L<sub>93</sub>, which has the nucleotide sequence SEQ ID NO:36 (the coding strand) and SEQ ID

NO:37 (the complementary strand). Alignment of nucleic acid molecules nCaFlt3L<sub>985</sub> and nCaFlt3L<sub>1019</sub> indicates the presence of an insertion of 91 nucleotides in nCaFlt3L<sub>1019</sub>. The insertion spans nucleotide 107 through nucleotide 198 of nCaFlt3L<sub>1019</sub>. A stop codon is found in this insertion in frame with the predicted initiation codon, which span

5 nucleotide 74 through nucleotide 76 of SEQ ID NO:6. Since this insertion (with an in-frame stop codon) occurs in or close to the signal peptide, it is likely that nucleic acid molecule nCaFlt3L<sub>1019</sub> encodes a nonfunctional Flt-3 ligand protein.

Comparison of nucleic acid sequence SEQ ID NO:6 with nucleic acid sequences reported in GenBank indicates that SEQ ID NO:6 showed the most homology, i.e., about

10 69.8% identity, with a human Flt-3 ligand gene. Comparison of amino acid sequence SEQ ID NO:7 with amino acid sequences reported in GenBank indicates that SEQ ID NO:7 showed the most homology, i.e. about 71% identity, with a human Flt-3 ligand protein. Sequence analysis was performed with DNAsis™ using the alignment settings of: gap penalty set at 5; number of top diagonals set at 5; fixed gap penalty set at 10; K-

15 tuple set at 2; window size set at 5 and floating gap penalty set at 10.

ii. This example describes the production of a recombinant molecule encoding a full length canine Flt-3 ligand protein and expression of that protein by a recombinant cell of the present invention.

A recombinant molecule, denoted herein as pCMV-nCaFlt3L<sub>882</sub> and capable of

20 expressing a full length form of Flt-3 ligand, was produced as follows. Nucleic acid molecule nCaFlt3L<sub>882</sub> was digested with the restriction endonucleases *Eco*RI and *Xba*I, gel purified and ligated into pCMV-Int A (prepared by methods described in Example 1)

to produce recombinant molecule pCMV-nCaFlt3L<sub>882</sub>. Insert size and identity were confirmed by restriction digestion, PCR, and sequencing analyses.

Stable transfectants expressing the recombinant molecule pCMV-nCaFlt3L<sub>882</sub> were established in Chinese Hamster Ovary cells (CHO, available from ATCC) as follows. Briefly, six-well polystyrene tissue culture plates were seeded with approximately  $4 \times 10^5$  cells per well in 2 ml of MEM (available from Life Technologies, Gaithersburg, MD ) supplemented with 100 mM L-glutamine, gentamicin, and 10% FBS (TCM). Cells were grown to about 80% confluence (about 18 hr). The recombinant molecule to be transfected was prepared using the Qiagen Endotoxin-Free Plasmid Maxi Kit as per the manufacturer's instructions. The recombinant molecule was linearized with the restriction enzyme *PvuI*, extracted with phenol, and precipitated with isopropanol. The plasmid pcDNA 3, available from Invitrogen, which contains the neomycin resistance gene, was linearized with the restriction enzyme *EcoRI*. Approximately 1  $\mu$ g of recombinant plasmid DNA and 100 ng of pcDNA3 were mixed with about 100  $\mu$ l OptiMEM medium, available from Life Technologies. About 10  $\mu$ l Lipofectamine (available from Life Technologies) was mixed with 100  $\mu$ l OptiMEM. The DNA-containing mixture was then added to the Lipofectamine mixture and incubated at room temperature for about 30 min. After incubation, about 800  $\mu$ l of OptiMEM was added, and the entire mixture was overlaid onto the CHO cells that had been rinsed with OptiMEM. Cells were incubated for 6 hours at 37°C, 5% CO<sub>2</sub>, 95% relative humidity. Approximately 1 ml of TCM with 20% FBS was added, and the cells were incubated overnight. The media was changed after about 24 hr. About 72 hr post transfection, the cells were split 1:4 and put into selection TCM containing 500  $\mu$ g/ml

Geneticin (G418), available from Life Technologies. The medium was changed every 3-5 days. After several weeks, G418-resistant colonies were trypsinized, and the cells were plated into 24 well plates. The resulting recombinant cells are referred to herein as CHO-pCMV-nCaFlt3L<sub>882</sub>. The recombinant cells were then expanded for testing.

- 5           iii.       The following describes the detection of expression of a canine Flt-3 ligand protein of the present invention by CHO-pCMV-nCaFlt3L<sub>882</sub>, a recombinant cell of the present invention.

Recombinant cells CHO-pCMV-nCaFlt3L<sub>882</sub>, produced as described in Example 2, part (B)(ii) above, were tested for surface expression of canine Flt-3 ligand using a cross-reactive goat anti-human Flt-3 ligand polyclonal antibody as follows. Briefly, 10   1 x 10<sup>5</sup> CHO-pCMV-nCaFlt3L<sub>882</sub> cells or CHO-pCMV cells (i.e., cells transfected with an empty vector as described in Example 1) were incubated in phosphate buffered saline (PBS) containing 30% fetal bovine serum (FBS) for about 30 min on ice. The cells were then spun down and treated with the following:

15

<u>Condition</u>	<u>Primary Incubation</u>	<u>Secondary Incubation</u>
1	PBS	Rabbit (Fab'2) anti sheep (H+L) FITC
2	Goat anti-human Flt3 ligand	Rabbit (Fab'2) anti sheep (H+L) FITC

Goat anti-human Flt3 ligand, available from R and D Systems, Minneapolis, MN was used at about 20µg/ml. Rabbit (Fab'2) anti sheep (H+L) FITC, available from Southern Biotechnology Associates, Inc., was used at about 10 µg/ml. These reagents were diluted 20   in PBS/5%FBS. All incubations were in 50 µl for about 1 hr on ice with 2 washes of PBS/5%FBS in between each incubation. Cells were then analyzed on a flow cytometer

(e.g., MoFlow Desk Top System, available from Cytomation, Ft. Collins, CO) with the fluorescein gate set at  $10^1$ . The results are shown below in Table 4.

Table 4. Expression of canine Flt3 ligand on CHO transfectants.

Cells	% positive	
	<u>Condition 1</u>	<u>Condition 2</u>
CHO-pCMV	1	1
CHO-pCMV nCaFlt3L <sub>882</sub>	2	48
CHO-pCMV nCaFlt3L <sub>882</sub>	1	20

Table 4 shows that canine Flt3 ligand is expressed on the surface of the CHO transfectants.

#### B. Feline Flt-3 ligand nucleic acid molecules and proteins.

This example describes the production of certain feline Flt-3 ligand nucleic acid molecules and proteins of the present invention.

A nucleic acid molecule encoding a feline Flt 3 ligand was isolated from a feline PBMC cDNA library as follows. A *Felis catus* mitogen activated PBMC cDNA library was constructed in the Uni-Zap-R XR™ vector, available from Stratagene, La Jolla, Ca, using Stratagene's Zap-cDNA-R™ Synthesis Kit and the manufacturer's protocol using mRNA isolated from *F. catus* peripheral blood mononuclear cells about 4 hours after they were activated by a polyclonal activating agent in culture. PCR amplification to isolate a feline Flt 3 ligand nucleic acid molecule was conducted according to the following set of steps: one initial denaturation step at 95°C for 3 minutes; then 35 cycles of the following: 94°C for 30 seconds, 53.8°C for 30 seconds, and 72°C for 105 seconds; then one final extension step at 72°C for 8 minutes. A 395-nucleotide cDNA fragment



containing the 5' end of feline Flt3 ligand coding region, denoted nFeFlt3L<sub>395</sub>, was amplified from the feline PMBC cDNA library using the following primers: vector primer T3 having nucleic acid sequence 5' AATTAACCCT CACTAAAGGG 3' (SEQ ID NO:142) (available from Stratagene) and the antisense primer having SEQ ID NO:14, described in Example 2A. The nucleic acid sequence of the coding strand of nFeFlt3L<sub>395</sub> is denoted SEQ ID NO:41. A 793-nucleotide cDNA fragment containing the 3' end of feline Flt3 ligand coding region, denoted nFeFlt3L<sub>793</sub>, was isolated using sense primer 2 having the nucleic acid sequence 5' CACAGYCCCA TCTCCTCC 3' (where Y was either T or C) denoted herein as SEQ ID NO:151, in conjunction with vector primer T7 having the nucleic acid sequence 5' GTAATACGAC TCACTATAGG GC 3' (SEQ ID NO:152). The nucleic acid sequence of the coding strand of nFeFlt3L<sub>793</sub> is denoted SEQ ID NO:42. Nucleic acid molecules nFeFlt3L<sub>395</sub> and nFeFlt3L<sub>793</sub> overlap by 246 nucleotides and form a composite sequence encoding a Flt3 ligand protein that is similar in length to that of PCaFlt3L<sub>294</sub>. This composite feline Flt3 ligand cDNA is referred to herein as nFeFlt3L<sub>942</sub>, the coding strand of which was shown to have nucleic acid sequence SEQ ID NO:43. The reverse complement of SEQ ID NO:43 is referred to herein as SEQ ID NO:45. Translation of SEQ ID NO:43 suggests that nucleic acid molecule nFeFlt3L<sub>942</sub> encodes a Flt3 ligand protein of 291 amino acids, denoted herein as PFeFlt3L<sub>291</sub>, the amino acid sequence of which is presented in SEQ ID NO:44, assuming an open reading frame having an initiation codon spanning from nucleotide 31 through nucleotide 33 of SEQ ID NO:43 and a stop codon spanning from nucleotide 904 through nucleotide 906 of SEQ ID NO:43. The coding region encoding PFeFlt3L<sub>291</sub>, not including the termination codon, is presented herein as nFeFlt3L<sub>873</sub>, which has the

nucleotide sequence SEQ ID NO:46 (the coding strand) and SEQ ID NO:47 (the complementary strand). A putative signal sequence coding region extends from nucleotide 31 to nucleotide 108 of SEQ ID NO:43. The proposed mature protein, denoted herein as PFeFlt3L<sub>265</sub>, denoted SEQ ID NO:49, contains about 265 amino acids, extending from residue 27 through residue 291 of SEQ ID NO:44. The nucleic acid molecule encoding PFeFlt3L<sub>265</sub> is denoted herein as nFeFlt3L<sub>795</sub>, (SEQ ID NO:48) extending from nucleotide 109 through nucleotide 903 of SEQ ID NO:43. SEQ ID NO:48 has a complementary strand denoted SEQ ID NO:50.

Sequence alignment indicates that nucleic acid sequence SEQ ID NO:43 shares the highest (67.8%) identity with the nucleic acid sequence of human Flt-3 ligand (GenBank accession numbers U04806 and U03858). Amino acid sequence SEQ ID NO:44 shares the highest (70.2%) identity with human Flt-3 ligand protein (GenBank accession numbers U04806 and U03858).

### Example 3.

This example describes the isolation and sequencing of certain canine CD40 and feline CD40 nucleic acid molecules and proteins of the present invention.

#### A. Canine CD40 nucleic acid molecules and proteins

This example describes the production of certain canine CD40 nucleic acid molecules and proteins of the present invention.

A canine CD40 nucleic acid molecule of the present invention was produced by PCR amplification as follows. A 321-nucleotide canine CD40 nucleic acid molecule, denoted nCaCD40<sub>321</sub>, was amplified from a canine PBMC cDNA library, prepared as described in Example 1, using two degenerate oligonucleotide primers designed in

accordance with conserved regions of human, bovine, rabbit, and mouse CD40 gene sequences available in GenBank: sense primer, 5' TGCCCRSTCG GCTTCTTCTC C 3', denoted herein as SEQ ID NO:128; and antisense primer, 5' CGACTCTCTT TRCCRTCCTC CTG 3', denoted herein as SEQ ID NO:129, where R was either A or G and S was either G or C. PCR conditions were as follows: one initial denaturation step at 95°C for 3 minutes; then 35 cycles of the following: 94°C for 30 seconds, then 53°C for 30 seconds, then 72°C for 105 seconds; followed by one final extension at 72°C for 5 minutes. The resulting PCR product, i.e., nCaCD40<sub>321</sub>, with a coding strand represented by SEQ ID NO:51, was radiolabeled using standard techniques and used to screen the canine PBMC cDNA library, under the following hybridization conditions: hybridized in 6X SSC, 5X Denhardt's solution, 0.5% SDS, 100 µg/ml single stranded DNA, 100 µg/ml tRNA for 36 hours at 68°C, followed by a wash of 0.1% SDS, 1X SSC at 55°C for 60 minutes. A clone (Clone 18B) containing a 1425-nucleotide canine CD40 nucleic acid molecule, denoted nCaCD40<sub>1425</sub>, was obtained. The nucleic acid sequence of the coding strand of nCaCD40<sub>1425</sub> is represented as SEQ ID NO:52. The reverse complement of SEQ ID NO:52 is referred to herein as SEQ ID NO:54. Translation of SEQ ID NO:52 suggests that nucleic acid molecule nCaCD40<sub>1425</sub> encodes a canine CD40 protein of 274 amino acids, denoted herein as PCaCD40<sub>274</sub>, the amino acid sequence of which is presented in SEQ ID NO:53, assuming an open reading frame having an initiation codon spanning from nucleotide 196 through nucleotide 198 of SEQ ID NO:52 and a stop codon spanning from nucleotide 1018 through nucleotide 1020 of SEQ ID NO:52. The coding region encoding PCaCD40<sub>274</sub>, not including the termination codon, is presented herein as

nCaCD40<sub>822</sub>, which has the nucleotide sequence SEQ ID NO:55 (the coding strand) and SEQ ID NO:56 (the complementary strand).

A putative signal sequence coding region extends from nucleotide 196 through nucleotide 252 of SEQ ID NO:52. The proposed mature protein, denoted herein as

5 PCaCD40<sub>255</sub>, represented by SEQ ID NO:58, contains about 255 amino acids, extending from residue 20 through residue 274 of SEQ ID NO:53. The nucleotide sequence encoding PCaCD40<sub>255</sub>, which extends from nucleotide 253 through nucleotide 1017 of SEQ ID NO:52, is denoted herein as nucleic acid molecule nCaCD40<sub>765</sub>, represented by SEQ ID NO:57 (the coding strand) and SEQ ID NO:59 (the complement strand).

10 Sequence analysis was performed with DNAsis™ using the alignment settings of: gap penalty set at 5; number of top diagonals set at 5; fixed gap penalty set at 10; k-tuple set at 2; window size set at 5 and floating gap penalty set at 10. At the amino acid level, PCaCD40<sub>274</sub> shares 65.3%, 50.1%, and 42.3% identity with the CD40 proteins of human, bovine, and mouse, respectively (Stamenkovic et al., *EMBO J.*, vol. 8:1403-1410, 1989; 15 Hirano et al., *Immunology*, vol. 90, pp. 294-300, 1997; Grimaldi et al., *J. Immunol.*, vol. 143, pp.3921-3926; Torres and Clark, *J. Immuno.*, vol. 148, pp. 620-626). At the nucleotide level, nCaCD40<sub>1425</sub> shares 69.3%, 69.4%, and 40.4% identity with the cDNA sequences of human, bovine, and mouse CD40, respectively.

#### B. Feline CD40 nucleic acid molecules and proteins

20 This example describes the isolation and sequencing of certain nucleic acid molecules of the present invention that encode certain feline CD40 proteins of the present invention.

A 336-nucleotide feline CD40 nucleic acid molecule, denoted nFeCD40<sub>336</sub>, was amplified from a feline PBMC cDNA library, prepared as described in Example 2, using PCR conditions and primers as described in Example 3A, i.e., a sense primer having SEQ ID NO:128; and an antisense primer having SEQ ID NO:129. The resulting PCR product, i.e., nFeCD40<sub>336</sub>, was shown to have a coding strand the nucleic acid sequence of which is represented as SEQ ID NO:60. The reverse complement of SEQ ID NO:60 is referred to herein as SEQ ID NO:62. Translation of SEQ ID NO:60 suggests that nucleic acid molecule nFeCD40<sub>336</sub> encodes a partial CD40 protein of 112 amino acids, denoted herein as PFeCD40<sub>112</sub>, the amino acid sequence of which is presented in SEQ ID NO:61, assuming an open reading frame spanning from nucleotide 1 through nucleotide 336 of SEQ ID NO:60.

Comparison of nucleic acid sequence SEQ ID NO:60 with nucleic acid molecules reported in GenBank indicates that SEQ ID NO:60 showed the most homology, i.e. 67.2% identity, with a human CD40 gene. Comparison of amino acid sequence SEQ ID NO:61 with amino acid sequences reported in GenBank indicates that SEQ ID NO:61 showed the most homology, i.e. about 54.4% identity, with a human CD40 protein. Sequence analysis was performed using the GCG GAP program as described above.

#### Example 4

This example describes the isolation and sequencing of certain canine CD154 (canine CD40 ligand) and feline CD154 (feline CD40 ligand) nucleic acid molecules and proteins of the present invention.

A. Canine CD154 (CD40 ligand) nucleic acid molecules and proteins

The following describes the isolation and sequencing of certain cDNA nucleic acid molecules encoding certain canine CD154 (CD40 ligand) proteins of the present invention.

5           A canine CD154 nucleic acid molecule of the present invention was produced by PCR amplification as follows. A 390-nucleotide canine CD40 nucleic acid molecule, denoted nCaCD154<sub>390</sub>, was amplified from a canine PBMC cDNA library, prepared as described in Example 1, using two degenerate oligonucleotide primers designed in accordance with human CD154 gene sequences available in GenBank: sense primer,

10   5' CCTCAAATTG CGGCACATGT C 3', denoted herein as SEQ ID NO:130; and antisense primer, 5' CTGTTTCAGAG TTTGAGTAAG CC 3', denoted herein as SEQ ID NO:131. PCR conditions used for canine CD154 cDNA amplification were standard conditions for PCR amplification (Sambrook, et al., *ibid.*). The resulting PCR product, i.e., nCaCD154<sub>390</sub>, with a coding strand represented by SEQ ID NO:63, was radiolabeled

15   using standard techniques and used to screen the canine PBMC cDNA library, under the hybridization conditions described in Example 3. A clone containing a 1878-nucleotide canine CD154 nucleic acid molecule, denoted nCaCD154<sub>1878</sub>, was obtained. The nucleic acid sequence of the coding strand of nCaCD154<sub>1878</sub> is represented as SEQ ID NO:64. The reverse complement of SEQ ID NO:64 is referred to herein as SEQ ID NO:66.

20   Translation of SEQ ID NO:64 suggests that nucleic acid molecule nCaCD154<sub>1878</sub> encodes a CD154 protein of 260 amino acids, denoted herein as PCaCD154<sub>260</sub>, the amino acid sequence of which is presented in SEQ ID NO:65, assuming an open reading frame having an initiation codon spanning from nucleotide 284 through nucleotide 286 of SEQ

ID NO:64 and a stop codon spanning from nucleotide 1064 through nucleotide 1066 of SEQ ID NO:64. The coding region encoding PCaCD154<sub>260</sub>, not including the termination codon, is presented herein as nCaCD154<sub>780</sub>, which has the nucleotide sequence SEQ ID NO:67 (the coding strand) and SEQ ID NO:68 (the complementary strand).

5           A putative signal/membrane anchor sequence coding region extends from nucleotide 284 through nucleotide 430 of SEQ ID NO:64. The proposed soluble CD154 protein, denoted herein as PCaCD154<sub>211</sub>, represented by SEQ ID NO:70, contains about 211 amino acids, extending from residue 50 through residue 260 of SEQ ID NO:65. The nucleotide sequence encoding PCaCD154<sub>211</sub>, which extends from nucleotide 431 through  
10   nucleotide 1063 of SEQ ID NO:64, is denoted herein as nucleic acid molecule nCaCD154<sub>633</sub>, represented by SEQ ID NO:69 (the coding strand) and SEQ ID NO:71 (the complement strand).

Sequence analysis was performed with DNAsis™ using the alignment settings of: gap penalty set at 5; number of top diagonals set at 5; fixed gap penalty set at 10; k-tuple  
15   set at 2; window size set at 5 and floating gap penalty set at 10. At the amino acid level, PCaCD154<sub>260</sub> shares 78.0%, 77.6%, and 67.6% identity with the CD154 proteins of human, bovine, and mouse, respectively (Graf et al., *Eur. J. Immunol.*, vol. 22, pp. 3191-3194, 1992; Hollenbaugh, et al., *EMBO J.*, vol. 11:4313-4321, 1992; Gauchat et al., *FEBS lett.*, vol., 315, pp. 259-266, 1993; Mertens et al., *Immunogenetics*, vol. 42, pp.  
20   430-431; Armitage et al., *Nature*, vol. 357, pp. 80-82; 1992). At the nucleotide level, nCaCD154<sub>1878</sub> shares 81.1%, 81.5%, and 74.4% identity with the sequences of human, bovine, and mouse CD154 cDNAs, respectively.



B. Feline CD154 (CD40 ligand) nucleic acid molecules and proteins

This example describes the isolation and sequencing of certain nucleic acid molecules encoding certain feline CD154 (CD40 ligand) proteins of the present invention.

5 A feline CD154 nucleic acid molecule was isolated by PCR amplification from a feline PBMC cDNA library, prepared as described in Example 2, using Amplitaq DNA polymerase (available from PE Applied Biosystems Inc, Foster City, CA) under the following PCR protocol: one initial denaturation step at 95°C for 5 minutes; then 40 cycles of the following: 94°C for 45 seconds, then 48°C for 45 seconds, then 72°C for  
10 120 seconds; followed by a final extension at 72°C for 7 minutes. The forward and reverse primers used were based on human CD154 cDNA sequences outside the open reading frame in the 5' and 3' untranslated regions, respectively, so that the open reading frame in the PCR product contained only feline sequences. The sequence of the forward primer was 5'GAAGATACCA TTTCAACTTT AACACAGC 3' SEQ ID NO:132, and  
15 that of the reverse primer was 5' TGCTGTATTG TGAAGACTCC CAGC 3' SEQ ID NO:133. PCR products were cloned into the TA cloning vector (available from Invitrogen Corporation, Carlsbad, CA), and the resulting clones were sequenced using an ABI Prism™ Model 377 Automatic DNA Sequencer (available from PE Applied Biosystems Inc.). DNA sequencing reactions were performed using Prism™ dRhodamine  
20 Terminator Cycle Sequencing Ready Reaction kits (available from PE Applied Biosystems Inc.).

The PCR product was sequenced and found to contain 885 nucleotides, and is denoted as nFeCD154<sub>885</sub>. The nucleotide sequence of the coding strand of nFeCD154<sub>885</sub>

is represented herein as SEQ ID NO:72, and its complement is denoted SEQ ID NO:74.

Translation of the open reading frame in SEQ ID NO:72 suggests that nFeCD154<sub>885</sub>

encodes a protein containing 260 amino acids, referred to herein as PFeCD154<sub>260</sub>, the

amino acid sequence of which is presented as SEQ ID NO:73, assuming an open reading

5 frame in which the first codon spans from nucleotide 29 through nucleotide 31 of SEQ ID

NO:72, and the stop codon spans from nucleotide 809 through nucleotide 811 of SEQ ID

NO:72. The encoded protein has a predicted molecular weight of 28.6 kDa for the

precursor protein and 27.2 kDa for the mature protein. The coding region encoding

PFeCD154<sub>260</sub>, not including the termination codon, is presented herein as nFeCD154<sub>780</sub>,

10 which has the nucleotide sequence SEQ ID NO:75 (the coding strand) and SEQ ID

NO:76 (the complementary strand)

A putative signal/membrane anchor sequence coding region extends from

nucleotide 29 through nucleotide 175 of SEQ ID NO:72. The proposed soluble feline

CD154 protein, denoted herein as PFeCD154<sub>211</sub>, represented by SEQ ID NO:78, contains

15 about 211 amino acids, extending from residue 50 through residue 260 of SEQ ID NO:73.

The nucleotide sequence encoding PFeCD154<sub>211</sub>, denoted herein as nFeCD154<sub>633</sub> which

extends from nucleotide 176 through nucleotide 808 of SEQ ID NO:72, is represented

herein by SEQ ID NO:77 (the coding strand) and SEQ ID NO: 79 (the complementary

strand).

20 Comparison of feline CD154 nucleotide and amino acid sequences with those of

other species published in GenBank reveals that the feline CD154 nucleotide sequence

SEQ ID NO:75 is 86%, 88% and 75% identical to the human, bovine and murine CD154

gene sequences, respectively (Genbank accession number L07414, Z48469 and X56453

respectively). At the amino acid sequence level, SEQ ID NO:73 is 81%, 82%, and 67% identical to the human, bovine and murine CD154 amino acid sequences, respectively.

Hydrophobicity analysis of feline CD154 proteins results in a pattern similar to those of human, bovine and murine CD154 proteins. A putative N-glycosylation site was

5 identified at position 239 in PFeCD154<sub>260</sub> that is conserved in the human, bovine and murine amino acid sequences. Five cysteine residues are present in the feline CD154 protein sequence SEQ ID NO:73. Four of the five residues, located at positions 72, 84, 177 and 217 of PFeCD154<sub>260</sub>, are conserved in all four species and are likely involved in disulfide bond formation. The cysteine residue located at position 193 of PFeCD154<sub>260</sub> is  
10 present in all but the murine sequence.

#### Example 5

This example describes the isolation and sequencing of certain canine IL-5 nucleic acid molecules and proteins of the present invention. This example also describes expression of canine IL-5 in a *Pichia* expression system and the bioactivity of such an  
15 expressed protein.

##### A. Isolation and sequencing of canine IL-5 nucleic acid molecules and proteins

A canine IL-5 cDNA nucleic acid molecule encoding a canine IL-5 protein was isolated by PCR amplification from a canine PBMC cDNA library (prepared as described  
20 in Example 1) using PCR conditions as described in Example 4B and the following primers. Degenerate oligonucleotide primers were designed in accordance with conserved regions of human and cat IL-5 gene sequences available in GenBank: sense primer, 5' ATGCACTTTC TTTGCC 3', denoted herein as SEQ ID NO:134; antisense

primer 1, 5' CTGGAGGAAA AKACTTCRAT GATTCTGATA TCTGAAATAT AT 3', denoted herein as SEQ ID NO:135; and antisense primer 2, 5' CTGACYCTTK STTGGSCCTC ATTCTCA 3', denoted herein as SEQ ID NO:136, where K was G or T, R was either A or G, S was either G or C, and Y was either T or C.

5 An about 610-nucleotide canine IL-5 nucleic acid molecule, denoted nCaIL-5<sub>610</sub>, was obtained using primers having SEQ ID NO:134 and SEQ ID NO:135, respectively. The sequence of the coding strand of nCaIL-5<sub>610</sub> is represented herein as SEQ ID NO:80. The reverse complement of SEQ ID NO:80 is referred to herein as SEQ ID NO:82.

Translation of SEQ ID NO:80 suggests that nucleic acid molecule nCaIL-5<sub>610</sub> encodes an  
 10 IL-5 protein of 134 amino acids, denoted herein as PCaIL-5<sub>134</sub>, the amino acid sequence of which is presented in SEQ ID NO:81, assuming an open reading frame having an initiation codon spanning from nucleotide 29 through nucleotide 31 of SEQ ID NO:80 and a stop codon spanning from nucleotide 431 through nucleotide 433 of SEQ ID NO:80. The coding region encoding PCaIL-5<sub>134</sub>, not including the termination codon, is  
 15 presented herein as nCaIL-5<sub>402</sub>, which has the nucleotide sequence SEQ ID NO:83 (the coding strand) and SEQ ID NO:84 (the complementary strand).

An about 488-nucleotide fragment, denoted herein as nCaIL-5<sub>488</sub>, isolated by PCR with primers having SEQ ID NO:134 and SEQ ID NO:136, respectively, corresponds to nucleotide 1 through nucleotide 488 of nCaIL-5<sub>610</sub>.

20 A putative signal sequence coding region extends from nucleotide 29 through nucleotide 85 of SEQ ID NO:80. The proposed mature protein, denoted herein as PCaIL-5<sub>115</sub>, represented by SEQ ID NO:86, contains about 115 amino acids, extending from residue 20 though residue 134 of SEQ ID NO:81. The nucleotide sequence encoding

PCaIL-5<sub>115</sub>, which extends from nucleotide 86 through nucleotide 430 of SEQ ID NO:80, is denoted herein as nucleic acid molecule nCaIL-5<sub>345</sub>, represented by SEQ ID NO:85 (coding strand) and SEQ ID NO:87 (the complement strand).

Sequence analysis was performed with DNAsis™ using the alignment settings of:

- 5 gap penalty set at 5; number of top diagonals set at 5; fixed gap penalty set at 10; k-tuple set at 2; window size set at 5 and floating gap penalty set at 10. At the amino acid level, PCaIL-5<sub>134</sub> shared 82.8% and 57.4% identity with feline and human IL-5 proteins, respectively (Padrid et al., *Am. J. Vet. Res.*, vol. 59, pp. 1263-1269, 1998; Azuma et al., *Nucleic Acids Res.*, vol. 14, pp. 9149-9158, 1986). At the nucleotide level, nCaIL-5<sub>610</sub>
- 10 shared 81.7% and 75% identity with the cDNA sequences of the feline and human IL-5, respectively.

#### B. Expression of canine IL-5 in *Pichia*

- This example describes the expression in *Pichia* of a canine IL-5 cDNA fragment, namely a canine IL-5 nucleic acid molecule denoted nCaIL-5<sub>348</sub>, the coding strand of
- 15 which consists of nucleotides 86-433 of SEQ ID NO:80, and as such, encodes a predicted mature canine IL-5 protein having SEQ ID NO:86. Nucleic acid molecule nCaIL-5<sub>348</sub>, was PCR amplified from nCaIL-5<sub>610</sub> using sense primer 5' GGGCTCGAGA
  - AAAGATTTCG TGTAGAAAAT CCCATG 3' denoted herein as SEQ ID NO:137, with nucleotides 16-36 corresponding to nucleotides 86-106 of SEQ ID NO:80; and antisense
  - 20 primer 5' CCCGCGGCCG CTCAACTTTC CGGTGTCCAC TC 3', denoted herein as SEQ ID NO:138, with nucleotides 12-32 corresponding to the reverse complement of nucleotides 413-433 of SEQ ID NO:80. To facilitate cloning, an *Xho*I site (shown in

bold) was added to the sense primer and a *NotI* site (shown in bold) was added to the antisense primer. The PCR-amplified fragment was digested with restriction endonucleases *XhoI* and *NotI*, gel purified and ligated into pPICZ $\alpha$ A plasmid vector, available from Invitrogen, that had been digested by *XhoI* and *NotI* and gel purified, to  
 5 produce recombinant molecule pPICZ $\alpha$ A-nCaIL-5<sub>348</sub>. The insert in the recombinant molecule was verified by DNA sequencing. The recombinant molecule was used to transform *Pichia pastoris* strain X-33 by electroporation to produce recombinant cell *Pichia*-pPICZ $\alpha$ A-nCaIL-5<sub>348</sub>. Recombinant cell *Pichia*-pPICZ $\alpha$ A-nCaIL-5<sub>348</sub> was cultured using techniques known to those skilled in the art and IL-5 expression was  
 10 induced with methanol. The supernatant was recovered and submitted to SDS-PAGE. Silver staining of the resultant gel indicated a band of about 18 kDa only seen in the supernatant of *Pichia* transformed with recombinant molecule pPICZ $\alpha$ A-nCaIL-5<sub>348</sub>.

### C. Bioactivity of *Pichia*-expressed canine IL-5

The following describes a bioassay to detect the expression of canine IL-5 by  
 15 stimulating the proliferation of TF-1 cells.

TF-1 cells, grown and maintained as described in Example 1E, were extensively washed to remove rhuGM-CSF, and then added at approximately  $1 \times 10^4$  cells per well to 96-well flat bottom plates. *Pichia*-expressed canine IL-5, produced as described in Example 5B, was dialyzed overnight at 4° C against Phosphate Buffered Saline, diluted to  
 20 the appropriate concentration in TCM-TF-1 without rhuGM-CSF and filter sterilized. Cells and *Pichia*-produced canine IL-5 were incubated for 48 hours in 5% CO<sub>2</sub> at 37°C, then pulsed, incubated, harvested and counted as described in Example 1E. The results are shown in Table 5.

Table 5. Stimulation of proliferation of TF-1 with *Pichia*-expressed canine IL-5

	<u>1/dilution</u>	<u>Counts per minute</u>
5	2	44,885
	4	101,564
	8	81,161
	16	59,384
	32	40,508
	64	15,948
10	128	6,634
	256	2,441
	Media (no IL-5)	172

Table 5 shows that canine IL-5 expressed by *Pichia* is biologically active, as demonstrated by its ability to stimulate proliferation of TF-1 cells.

#### Example 6

15 This example describes the isolation and sequencing of certain canine IL-13 nucleic acid molecules and proteins of the present invention. This example also describes expression of canine IL-13 in *E. coli* and bioactivity of such an expressed protein.

#### A. Isolation and sequencing of canine IL-13 nucleic acid molecules and proteins

20 A canine IL-13 cDNA nucleic acid molecule encoding a canine IL-13 protein was isolated by PCR amplification from a canine PBMC cDNA library (prepared as described in Example 1) using the following primers and PCR conditions: Degenerate oligonucleotide primers were designed in accordance with conserved regions of human and cat IL-5 gene sequences available in GenBank: sense primer, 5' GTCMTKGCTC  
25 TYRCTTGCCT TGG 3', denoted herein as SEQ ID NO:139; antisense primer 1, 5' AASTGGGCY ACYTCGATTT TGG 3', denoted herein as SEQ ID NO:140; antisense primer 2, 5' GTGATGTTGM YCAGCTCCTC 3', denoted herein as SEQ ID



NO:141, where M was either A or C, K was G or T, R was either A or G, S was either G or C, and Y was either T or C. PCR conditions used were as follows: One initial denaturation step at 95°C for 3 minutes; then 38 cycles of the following: 94°C for 30 seconds, 51.8°C for 45 seconds, then 72°C for 105 seconds; then a final extension at 5 72°C for 5 minutes.

An about 272-nucleotide canine IL-13 nucleic acid molecule, denoted nCaIL-13<sub>272</sub> and having a coding strand represented by SEQ ID NO:89, was PCR amplified using primers having nucleic acid sequences of SEQ ID NO:139 and SEQ ID NO:140, respectively. An about 166-nucleotide canine IL-13 nucleic acid molecule, denoted 10 nCaIL-13<sub>166</sub> and having a coding strand represented by SEQ ID NO:88, was isolated using primers having nucleic acid sequences of SEQ ID NO:142 (see Example 2B) and SEQ ID NO:141, respectively. Nucleic acid molecules nCaIL-13<sub>272</sub> and nCaIL-13<sub>272</sub> form a overlapping composite fragment of 383 nucleotides, denoted nCaIL-13<sub>383</sub>. Two canine IL-13 specific primers (i.e., sense primer, 5' ATGGCGCTCT GGTGACTGT 3', 15 denoted herein as SEQ ID NO:143; and antisense primer, 5' GGCTTTTGAG AGCACAGTGC 3', denoted herein as SEQ ID NO:144) were derived from nCaIL-13<sub>383</sub> and were used to isolate a 278-nucleotide fragment, denoted nCaIL-13<sub>278</sub> and having a coding strand represented by SEQ ID NO:90. Nucleic acid molecule nCaIL-13<sub>278</sub> was radiolabeled and used to screen the canine PBMC cDNA library under the following 20 hybridization conditions: hybridization took place in 6X SSC, 5X Denhardt's solution, 0.5% SDS, 100 µg/ml single stranded DNA, 100 µg/ml tRNA, for 36 hours at 60°C; the final wash solution was 0.1% SDS, 0.125X SSC at 60°C for 30 minutes. Two clones were selected, namely clone 80 and clone 78.

Sequence analysis of Clone 80 indicated that the clone includes an about 1302-nucleotide canine IL-13 nucleic acid molecule referred to herein as nCaIL-13<sub>1302</sub>, the coding strand of which was shown to have nucleic acid sequence SEQ ID NO:91. The reverse complement of SEQ ID NO:91 is referred to herein as SEQ ID NO:93.

- 5 Translation of SEQ ID NO:91 suggests that nucleic acid molecule n nCaIL-13<sub>1302</sub> encodes an IL-13 protein of 131 amino acids, denoted herein as PCaIL-13<sub>131</sub>, the amino acid sequence of which is presented in SEQ ID NO:92, assuming an open reading frame having an initiation codon spanning from nucleotide 52 through nucleotide 54 of SEQ ID NO:91 and a stop codon spanning from nucleotide 445 through nucleotide 447 of SEQ ID
- 10 NO:91. The coding region encoding PCaIL-13<sub>131</sub>, not including the termination codon, is presented herein as nCaIL-13<sub>393</sub>, which has the nucleotide sequence SEQ ID NO:94 (the coding strand) and SEQ ID NO:95 (the complementary strand).

- A putative signal sequence coding region extends from nucleotide 52 to nucleotide 111 of SEQ ID NO:91. The proposed mature protein, denoted herein as
- 15 PCaIL-13<sub>111</sub>, represented by SEQ ID NO:97, contains 111 amino acids, extending from residue 21 through residue 131 of SEQ ID NO:91. The nucleotide sequence encoding PCaIL-13<sub>111</sub>, which extends from nucleotide 112 through nucleotide 444 of SEQ ID NO:91, is denoted herein as nucleic acid molecule nCaIL-13<sub>333</sub>, represented by SEQ ID NO:96 (coding strand) and SEQ ID NO:98 (the complement strand).

- 20 Sequence analysis of Clone 78 indicated that the clone includes an about 1269-nucleotide canine IL-13 nucleic acid molecule referred to herein as nCaIL-13<sub>1269</sub>, the coding strand of which was shown to have nucleic acid sequence SEQ ID NO:99. The reverse complement of SEQ ID NO:99 is referred to herein as SEQ ID NO:101.

Translation of SEQ ID NO:99 suggests that nucleic acid molecule nCaIL-13<sub>1269</sub> encodes an IL-13 protein of 130 amino acids, denoted herein as PCaIL-13<sub>130</sub>, the amino acid sequence of which is presented in SEQ ID NO:100, assuming an open reading frame having an initiation codon spanning from nucleotide 57 through nucleotide 59 of SEQ ID NO:99 and a stop codon spanning from nucleotide 447 through nucleotide 449 of SEQ ID NO:99. The coding region encoding PCaIL-13<sub>130</sub>, not including the termination codon, is represented herein as nCaIL-13<sub>390</sub>, which has the nucleotide sequence SEQ ID NO:102 (the coding strand) and SEQ ID NO:103 (the complementary strand). PCaIL-13<sub>130</sub> is missing one amino acid compared to PCaIL-13<sub>133</sub>, namely amino acid position Q97 of PCaIL-13<sub>133</sub>.

A putative signal sequence coding region extends from nucleotide 57 to nucleotide 116 of SEQ ID NO:99. The proposed mature protein, denoted herein as PCaIL-13<sub>110</sub>, represented by SEQ ID NO:105, contains 110 amino acids, extending from residue 21 through residue 130 of SEQ ID NO:100. The nucleotide sequence encoding PCaIL-13<sub>110</sub>, which extends from nucleotide 117 through nucleotide 446 of SEQ ID NO:99, is denoted herein as nucleic acid molecule nCaIL-13<sub>330</sub>, represented by SEQ ID NO:104 (coding strand) and SEQ ID NO:106 (the complement strand).

Sequence analysis was performed with DNAsis™ using the alignment settings of: gap penalty set at 5; number of top diagonals set at 5; fixed gap penalty set at 10; k-tuple set at 2; window size set at 5 and floating gap penalty set at 10. At the amino acid level, PCaIL-13<sub>131</sub> shared 61.7%, 39.6%, 36.6% identity with the IL-13 proteins of human, mouse, and rat (Brown et al., *J. Immunol.*, vol. 142, pp. 679-687, 1989; Lakkis et al., *Biochem. Biophys. Res. Commun.*, Vol. 197, pp. 612-618, 1993; McKenzie et al., *Proc.*

*Natl Acad. Sci. USA*, vol. 90, pp. 3735-3739, 1993; Minty et al., *Nature*, vol. 362, pp. 248-250, 1993), respectively. At the nucleotide level, nCaIL-13<sub>1302</sub> shared 56.0%, 57.1%, and 45.9% identity with the sequences of human, rat, and mouse IL-13 cDNAs, respectively.

## 5            B.        Expression of canine IL-13 in *E. coli*

This example describes the expression in *E. coli* of a canine IL-13 cDNA fragment, namely a canine IL-13 nucleic acid molecule denoted nCaIL-13<sub>336</sub>, the coding strand of which consists of nucleotides 112-447 of SEQ ID NO:91, and as such, encodes a predicted mature canine IL-13 protein having SEQ ID NO:97. Nucleic acid molecule

10    nCaIL-13<sub>336</sub> was PCR amplified from nCaIL-13<sub>1302</sub> using sense primer

5' CCCCATATGA GCCCTGTGAC TCCCTCCCC 3' denoted herein as SEQ ID:145, with nucleotides 10-29 corresponding to nucleotides 112-1131 of SEQ ID NO:91; and antisense primer 5' GGGGAATTCT CATCTGAAAT TTCCATGGCG 3', denoted herein as SEQ ID NO:146, with nucleotides 10-30 corresponding to the reverse

15    complement of nucleotides 427-447 of SEQ ID NO:91. To facilitate cloning, an *Nde*I site (shown in bold) was added to the sense primer and an *Eco*RI site (shown in bold) was added to the antisense primer. The resulting PCR fragment was digested with restriction endonucleases *Nde*I and *Eco*RI, gel purified and ligated into  $\lambda$ cro plasmid vector, the production of which is described in U.S. Patent No. 5,569,603 by Tripp et al., issued

20    October 29, 1996, that had been digested by *Nde*I and *Eco*RI and gel purified to produce recombinant molecule p $\lambda$ cro-nCaIL-13<sub>336</sub>. The insert in the recombinant molecule was verified by DNA sequencing. Recombinant molecule p $\lambda$ cro-nCaIL-13<sub>336</sub> was used to

transform *E. coli* strain HCE101 (BL21), thereby producing BL21-p $\lambda$ cro-nCaIL-13<sub>336</sub>. PCaIL-13<sub>111</sub> was produced under conditions as described in U.S. Patent No. 5,569,603, *ibid.*, protein expression being induced by switching the fermentation temperature from 32°C to 42°C. SDS-PAGE and Commassie blue staining analysis indicated that a band of about 11 kD was only produced by induced BL21-p $\lambda$ cro-nCaIL-13<sub>336</sub> recombinant cells. The 11-kD band showed a positive reaction with a rabbit polyclonal antibody against human IL-13 (available from PeproTech Inc, Rocky Hill, NJ), indicating expression of canine IL-13 in *E. coli*.

#### C. Bioactivity of *E. coli*-expressed canine IL-13

The following describes a bioassay to detect the expression of canine IL-13 by stimulating the proliferation of TF-1 cells.

TF-1 cells, grown and maintained as described in Example 1E, were extensively washed to remove rhuGM-CSF, and then added at approximately  $1 \times 10^4$  cells per well to 96-well flat bottom plates. *E. coli*-produced PCaIL-13<sub>111</sub>, produced as described in Example 6B, was dialyzed overnight at 4° C against Phosphate Buffered Saline, diluted to the appropriate concentration in TCM-TF-1 without rhuGM-CSF and filter sterilized. Cells and *E. coli*-produced PCaIL-13<sub>111</sub> were incubated for 48 hours in 5% CO<sub>2</sub> at 37°C, then pulsed, incubated, harvested and counted as described in Example 1E. The results are shown in Table 6.

Table 6. Stimulation of proliferation of TF-1 with *E. coli* PCaIL-13<sub>111</sub>

	<u>Concentration <i>E. coli</i> PCaIL-13<sub>111</sub></u> <u>(ng/ml)</u>	<u>Counts per minute</u>
5	1000	126,203
	500	77,893
	250	57,781
	125	40,491
	62.5	26,115
10	31.3	7,042
	15.6	8,713
	0	991

Table 6 shows that canine IL-13 expressed by *E. coli* is biologically active, as demonstrated by its ability to stimulate proliferation of TF-1 cells.

#### Example 7

15 This example describes the isolation and sequencing of feline interferon alpha nucleic acid molecules and proteins of the present invention. This example also describes expression of feline interferon alpha proteins of the present invention in *E. coli* and mammalian cells as well as the bioactivities of the resulting proteins.

#### A. Isolation and sequencing of feline IFN-alpha nucleic acids and proteins

20 Feline IFN-alpha nucleic acid molecules were PCR amplified from a feline cDNA library as follows. Total RNA was isolated from cat (kitten) mesenteric lymph node cells stimulated with PMA (phorbol myristate acetate) for 48 hours using Tri Reagent™ (available from Molecular Research Center, Cincinnati, Ohio). cDNA was made from the RNA using the cDNA synthesis kit containing Ready to Go -You Prime First-Strand  
25 Beads™ (available from Amersham Pharmacia Biotech, Piscataway, NJ). An aliquot of this cDNA was used as a template to isolate a feline IFN-alpha nucleic acid molecule by PCR amplification using Amplitaq DNA polymerase™ (available from PE Applied

Biosystems Inc, Foster City, CA) and the following primers and conditions. The sequence of the forward primer was 5' ATGGCGCTGC CCTCTTCCTT CTTG 3' (SEQ ID NO:143), and that of the reverse primer was 5' TCATTTCTCG CTCCTTAATC TTTTCTGC 3' (SEQ ID NO:148). The following PCR protocol was used: one initial  
 5 denaturation step at 95°C for 5 minutes; then 43 cycles of the following: 94°C for 45 seconds, then 47°C for 45 seconds, then 72°C for 120 seconds; followed by a final extension at 72°C for 7 minutes. PCR products were cloned into the TA cloning vector (available from Invitrogen Corporation) and the clones were sequenced using an ABI Prism™ Model 377 Automatic DNA Sequencer (available from PE Applied Biosystems  
 10 Inc.). DNA sequencing reactions were performed using Prism™ dRhodamine Terminator Cycle Sequencing Ready Reaction kits (available from PE Applied Biosystems Inc.). Five PCR products were generated and sequenced. These products were included, respectively, in Clones #1, #2, #3, #5, and #6.

Clone #2 includes a feline IFN-alpha nucleic acid molecule that is represented  
 15 herein as nFeIFN $\alpha_{567a}$ , the coding strand of which was shown to have a nucleic acid sequence denoted herein as SEQ ID NO:107. The complement of SEQ ID NO:107 is represented herein by SEQ ID NO:109. Translation of SEQ ID NO:107 suggests that nFeIFN $\alpha_{567a}$  encodes a protein containing 189 amino acids, referred to herein as PFeIFN $\alpha_{189a}$ , with an amino acid sequence denoted SEQ ID NO:108. The open reading  
 20 frame of SEQ ID NO:107 is assumed to be the following: the first codon spans from nucleotide 1 through nucleotide 3 and the last codon before the stop codon spans from nucleotide 565 to nucleotide 567 of SEQ ID NO:107. The encoded protein has a predicted molecular weight of 21 kDa. The putative signal peptide cleavage site occurs



between amino acid positions 23 and 24, based on homology with the human and canine interferon-alpha proteins. The proposed mature protein (i.e. feline IFN $\alpha$  protein from which the signal sequence has been cleaved), denoted herein as PFeIFN $\alpha_{166a}$ , contains about 166 amino acids, extending from residue 24 to residue 166 of SEQ ID NO:108; the amino acid sequence is denoted herein as SEQ ID NO:114. The nucleic acid molecule encoding PFeIFN $\alpha_{166a}$  is denoted herein as nFeIFN $\alpha_{498a}$ , the coding strand of which is represented by SEQ ID NO:113, and the complementary strand of which is represented by SEQ ID NO:115. A putative N-glycosylation site and an interferon alpha-beta-delta family signature motif are present at amino acid positions 102 and 145, respectively, of PFeIFN $\alpha_{189a}$ .

Clone #3 includes a feline IFN-alpha nucleic acid molecule that is represented herein as nFeIFN $\alpha_{567b}$ , the coding strand of which was shown to have a nucleic acid sequence denoted herein as SEQ ID NO:110. The complement of SEQ ID NO:110 is represented herein by SEQ ID NO:112. Translation of SEQ ID NO:110 suggests that nFeIFN $\alpha_{567b}$  encodes a protein containing 189 amino acids, referred to herein as PFeIFN $\alpha_{189b}$ , with an amino acid sequence denoted SEQ ID NO:111. The open reading frame of SEQ ID NO:110 is assumed to be the following: the first codon spans from nucleotide 1 through nucleotide 3 and the last codon before the stop codon spans from nucleotide 565 through nucleotide 567 of SEQ ID NO:110. The encoded protein has a predicted molecular weight of 21 kDa. The putative signal peptide cleavage site occurs between amino acid positions 23 and 24, based on homology with the human and canine interferon-alpha proteins. The proposed mature protein (i.e. feline IFN $\alpha$  protein from which the signal sequence has been cleaved), denoted herein as PFeIFN $\alpha_{166b}$ , contains

about 166 amino acids, extending from residue 24 to residue 166 of SEQ ID NO:111; the amino acid sequence is denoted herein as SEQ ID NO:117. The nucleic acid molecule encoding PFeIFN $\alpha_{166b}$  is denoted herein as nFeIFN $\alpha_{498b}$ , the coding strand of which is represented by SEQ ID NO:116, and complementary strand of which is represented by

5 SEQ ID NO:118. A putative N-glycosylation site and an interferon alpha-beta-delta family signature motif are present at amino acid positions 102 and 145, respectively, of PFeIFN $\alpha_{189b}$ .

Clone #1 includes a feline IFN-alpha nucleic acid molecule that is represented herein as nFeIFNa $_{567c}$ , the coding strand of which was shown to have a nucleic acid

10 sequence denoted herein as SEQ ID NO:155. The complement of SEQ ID NO:155 is represented herein by SEQ ID NO:157. Translation of SEQ ID NO:155 suggests that nFeIFNa $_{567c}$  encodes a protein containing 189 amino acids, referred to herein as PFeIFNa $_{189c}$ , with an amino acid sequence denoted SEQ ID NO:156. The open reading frame of SEQ ID NO:155 is assumed to be the following: the first codon spans from

15 nucleotide 1 through nucleotide 3 and the last codon before the stop codon spans from nucleotide 565 to nucleotide 567 of SEQ ID NO:155. The encoded protein has a predicted molecular weight of 21 kDa. The putative signal peptide cleavage site occurs between amino acid positions 23 and 24, based on homology with the human and canine interferon-alpha proteins. The proposed mature protein (i.e. feline IFNa protein from

20 which the signal sequence has been cleaved), denoted herein as PFeIFNa $_{166c}$ , contains about 166 amino acids, extending from residue 24 to residue 166 of SEQ ID NO:156; the amino acid sequence is denoted herein as SEQ ID NO:159. The nucleic acid molecule encoding PFeIFNa $_{166c}$  is denoted herein as nFeIFNa $_{498c}$ , the coding strand of which is

represented by SEQ ID NO:158, and the complementary strand of which is represented by SEQ ID NO:160. A putative N-glycosylation site and an interferon alpha-beta-delta family signature motif are present at amino acid positions 102 and 145, respectively, of PFeIFNa<sub>189c</sub>.

- 5            Clone #5 includes a feline IFN-alpha nucleic acid molecule that is represented herein as nFeIFNa<sub>582d</sub>, the coding strand of which was shown to have a nucleic acid sequence denoted herein as SEQ ID NO:161. The complement of SEQ ID NO:161 is represented herein by SEQ ID NO:163. Translation of SEQ ID NO:161 suggests that nFeIFNa<sub>582d</sub> encodes a protein containing 194 amino acids, referred to herein as
- 10    PFeIFNa<sub>194d</sub>, with an amino acid sequence denoted SEQ ID NO:162. The open reading frame of SEQ ID NO:161 is assumed to be the following: the first codon spans from nucleotide 1 through nucleotide 3 and the last codon before the stop codon spans from nucleotide 580 through nucleotide 582 of SEQ ID NO:161. The encoded protein has a predicted molecular weight of 21.5 kDa. The putative signal peptide cleavage site occurs
- 15    between amino acid positions 23 and 24, based on homology with the human and canine interferon-alpha proteins. The proposed mature protein (i.e. feline IFNa protein from which the signal sequence has been cleaved), denoted herein as PFeIFNa<sub>171d</sub>, contains about 171 amino acids, extending from residue 24 to residue 171 of SEQ ID NO:162; the amino acid sequence is denoted herein as SEQ ID NO:165. The nucleic acid molecule
- 20    encoding PFeIFNa<sub>171d</sub> is denoted herein as nFeIFNa<sub>513d</sub>, the coding strand of which is represented by SEQ ID NO:164, and the complementary strand of which is represented by SEQ ID NO:166. A putative N-glycosylation site and an interferon alpha-beta-delta

family signature motif are present at amino acid positions 102 and 145, respectively, of PFeIFNa<sub>194d</sub>.

Clone #6 includes a feline IFN-alpha nucleic acid molecule that is represented herein as nFeIFNa<sub>567e</sub>, the coding strand of which was shown to have a nucleic acid sequence denoted herein as SEQ ID NO:167. The complement of SEQ ID NO:167 is represented herein by SEQ ID NO:169. Translation of SEQ ID NO:167 suggests that nFeIFNa<sub>567e</sub> encodes a protein containing 189 amino acids, referred to herein as PFeIFNa<sub>189e</sub>, with an amino acid sequence denoted SEQ ID NO:168. The open reading frame of SEQ ID NO:167 is assumed to be the following: the first codon spans from nucleotide 1 through nucleotide 3 and the last codon before the stop codon spans from nucleotide 565 to nucleotide 567 of SEQ ID NO:167. The encoded protein has a predicted molecular weight of 21 kDa. The putative signal peptide cleavage site occurs between amino acid positions 23 and 24, based on homology with the human and canine interferon-alpha proteins. The proposed mature protein (i.e. feline IFNa protein from which the signal sequence has been cleaved), denoted herein as PFeIFNa<sub>166e</sub>, contains about 166 amino acids, extending from residue 24 to residue 166 of SEQ ID NO:167; the amino acid sequence is denoted herein as SEQ ID NO:171. The nucleic acid molecule encoding PFeIFNa<sub>166e</sub> is denoted herein as nFeIFNa<sub>498e</sub>, the coding strand of which is represented by SEQ ID NO:170, and the complementary strand of which is represented by SEQ ID NO:172. A putative N-glycosylation site and an interferon alpha-beta-delta family signature motif are present at amino acid positions 102 and 145, respectively, of PFeIFNa<sub>189e</sub>.

Comparison of the nucleic acid sequences of the five feline IFN-alpha nucleic acid molecules of the present invention indicated that the sequences, while being very similar (i.e., encoded proteins sharing from about 96% to 99% identity), exhibited several differences. The differences in nucleic acid sequences and deduced amino acid sequences are summarized in Table 7. The left hand column indicates the change at the nucleotide or amino acid level, as appropriate, and the "X"s in the other columns indicate which clones include such changes. For example, feline IFN-alpha protein PfeIFNa<sub>194d</sub> (having SEQ ID NO:161) has five extra amino acids (namely IHPED) inserted at position at 139 as compared to feline IFN-alpha proteins PfeIFNa<sub>189a</sub> (SEQ ID NO:108), PfeIFNa<sub>189b</sub> (SEQ ID NO:111), PfeIFNa<sub>189c</sub> (SEQ ID NO:155) or PfeIFNa<sub>189e</sub> (SEQ ID NO:167). Other variations, i.e., nucleotide substitutions, some of which lead to amino acid variations, are also indicated in Table 7.

Table 7. Comparison of feline IFN-alpha nucleic acid molecules and proteins

	Amino acid Changes	Clone # 1	Clone # 2	Clone # 3	Clone # 5	Clone # 6
5	5 amino acid deletion	X	X	X		X
	S <sub>18</sub> to S <sub>18</sub> (TCC to TCT)					X
	C <sub>52</sub> to C <sub>52</sub> (TGT to TGC)					X
10	R <sub>56</sub> to R <sub>56</sub> (AGA to AGG)			X		
	N <sub>57</sub> to S <sub>57</sub> (AAT to AGT)	X			X	
15	F <sub>66</sub> to F <sub>66</sub> (TTC to TTT)	X	X			
	A <sub>74</sub> to A <sub>74</sub> (GCC to GCT)			X		
	K <sub>86</sub> to E <sub>86</sub> (AAG to GAG)			X		
20	R <sub>115</sub> to W <sub>115</sub> (CGG to TGG)	X	X			
	L <sub>125</sub> to V <sub>125</sub> (CTG to GTG)			X	X	X
25	L <sub>125</sub> to M <sub>125</sub> (CTG to ATG)	X	X			
	L <sub>135</sub> to L <sub>135</sub> (CTG to CTC)	X	X	X		X
	I <sub>141</sub> to L <sub>141</sub> (ATC to CTC)			X		

30 Feline IFN-alpha proteins of the present invention PFeIFN $\alpha_{189a}$ , PFeIFN $\alpha_{189b}$ ,  
PFeIFN $\alpha_{189c}$ , and PFeIFN $\alpha_{189e}$  are five amino acids shorter than the GenBank entry for  
feline IFN-omega, accession # E02521, while IFN-alpha protein PFeIFN $\alpha_{194d}$  of the  
present invention has the same number of amino acids as the feline IFN-omega reported  
in GenBank. In addition, there are: 3 non-conservative and 2 conservative changes at the  
35 amino acid level between this GenBank entry and SEQ ID NO:108 (PFeIFN $\alpha_{189a}$ ); 4 non-  
conservative and 3 conservative changes at the amino acid level between this GenBank

entry and SEQ ID NO:111 (PfeIFN $\alpha_{189b}$ ); 4 non-conservative and 3 conservative changes at the amino acid level between this GenBank entry and SEQ ID NO:156 (PFeIFNa $_{189c}$ ); 2 non-conservative and 2 conservative changes at the amino acid level between this GenBank entry and SEQ ID NO:162 (PfeIFNa $_{194d}$ ); and 1 non-conservative and 5 conservative changes at the amino acid level between this GenBank entry and SEQ ID NO:168 (PFeIFNa $_{189e}$ ).

The lengths of SEQ ID NO:108 and SEQ ID NO:111, when compared with those of IFN-alpha proteins of other species, are two amino acids longer than published canine interferon-alpha subtype 1, 2 and 3 sequences, two amino acids longer than published human interferon-alpha type 1,B,D, F, and J sequences, three amino acids longer than the published human interferon-alpha sequence type A sequence and two amino acids longer than published murine interferon-alpha type B, 8, 7, 11, and 19 sequences. The lengths of SEQ ID NO:156 and SEQ ID NO:168, when compared with those of IFN-alpha proteins of other species, are two amino acids longer than published canine interferon-alpha subtype 1, 2 and 3 sequences, two amino acids longer than published human interferon-alpha type 1,B,D, F, and J sequences, three amino acids longer than the published human interferon-alpha sequence type A sequence and two amino acids longer than published murine interferon-alpha type B, 8, 7, 11, and 19 sequences. The length of SEQ ID NO:162, when compared with those of IFN-alpha proteins of other species, are seven amino acids longer than published canine interferon-alpha subtype 1, 2 and 3 sequences, seven amino acids longer than published human interferon-alpha type 1,B,D, F, and J sequences, eight amino acids longer than the published human interferon-alpha sequence



type A sequence and seven amino acids longer than published murine interferon-alpha type B, 8, 7, 11, and 19 sequences.

B. Expression of feline IFN-alpha proteins in mammalian cells

This example describes the expression of the feline IFN-alpha proteins of the present invention in Chinese hamster ovary (CHO) cells.

Feline IFN-alpha nucleic acid molecule PCR products were amplified from nFeIFN $\alpha_{567a}$ , nFeIFN $\alpha_{567b}$ , nFeIFN $\alpha_{567c}$ , nFeIFN $\alpha_{582d}$ , and nFeIFN $\alpha_{567e}$  using Pfu DNA polymerase<sup>TM</sup> (available from Stratagene, La Jolla, CA) and the following primers and conditions. The sequence of the forward primer was 5'ATTAGGATCC ATGGCGCTGC  
 10 CCTCTTCCT 3' (SEQ ID NO:173), and that of the reverse primer was 5'GCCTCTAGAC TGTCATTCT CGCTCCTTAA TCTTTTCTGC 3' (SEQ ID NO:174). The following PCR protocol was used: one initial denaturation step at 95°C for 5 minutes; then 30 cycles of the following: 94°C for 30 seconds, then 50°C for 30 seconds, then 72°C for 90 seconds; followed by a final extension at 72°C for 7 minutes.

15 Each of the five PCR products was ligated into a CMV-Int A-kan+(amp) expression vector using techniques similar to those described in Example 1Bii to produce recombinant molecules in which feline IFN-alpha nucleic acid molecules were operatively linked to transcription control sequences. It is to be noted that CMV-Int A-kan<sup>+</sup>(amp) vector is similar to the pCMV-Int A plasmid vector described in Example 1Bii  
 20 except that the ampicillin resistance gene open reading frame has been disrupted by the insertion of the kanamycin resistance gene. The feline IFN-alpha nucleic acid molecules in the recombinant molecules were sequenced using an ABI Prism<sup>TM</sup> Model 377 Automatic DNA Sequencer (available from PE Applied Biosystems Inc.). DNA

sequencing reactions were performed using Prism<sup>TM</sup> dRhodamine Terminator Cycle Sequencing Ready Reaction kits (available from PE Applied Biosystems Inc.). The sequence data indicated that there was no changes introduced during the PCR amplification or ligation in any of the nucleic acid molecules.

5           Using techniques similar to those described elsewhere herein, CHO cells were transiently transfected with each of the five recombinant molecules encoding a subtype of feline IFN-alpha protein using Lipofectamine<sup>TM</sup> (available from Life technologies, Inc.) resulting in recombinant cells expressing feline IFN-alpha subtype proteins of the present invention. The cells and culture supernatants were harvested 48 hours later and Western  
10       analysis was done using both pellets and the supernatants from each transfection. The detecting antibody was an anti-human IFN-alpha-A antibody (available from Accurate Chemical and Scientific Corporation, Westbury, NY). The Western analysis indicated that each of the five feline IFN-alpha nucleic acid molecule-containing recombinant cells expressed a corresponding feline IFN-alpha subtype protein which was secreted into the  
15       tissue culture supernatant and recognized by the antibody against human IFN-alpha-A. The migration patterns of each of the CHO cell-expressed feline IFN-alpha subtype proteins suggested that each of the proteins is glycosylated.

C.       Bioactivity of mammalian-expressed feline-IFN alpha proteins

(i)       The antiviral activity of the five CHO-expressed feline IFN-alpha subtype  
20       proteins, produced as described in Example 7B, was tested using the following protocol: Crandell feline kidney (CRFK) cells were treated for 24 hours, using procedures known to those skilled in the art, with or without IFN-alpha tissue culture supernatants, produced as described in Example 7B. The cells were then infected with feline calicivirus and

cytopathic effects induced by the virus were assessed 12 to 14 hours later using techniques known to those skilled in the art. The cell layers were fixed in methanol, stained with crystal violet and examined under the microscope or processed for the MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) assay. The MTT assay was conducted as follows. After viral infection, the infected cells were washed with PBS. A volume of MTT stock solution (5 mg/ml in PBS) equal to one-tenth of the original culture volume was added to each well being assayed and incubated at 37°C for 3 to 4 hr. The MTT solution was removed, and acidified isopropanol (0.1 N HCl in absolute isopropanol) was added to the wells to solubilize the converted dye. The absorbance of the converted dye was measured at 570 nm using a plate reader. Each of the five IFN-alpha subtype proteins demonstrated anti-viral activity. Pre-treatment with any of the subtypes of IFN-alpha proteins of the present invention resulted in significant reduction in the virus-induced cytopathic effect.

(ii) The CHO cell-expressed feline IFN-alpha subtype proteins were also tested for their ability to inhibit granulocyte-macrophage colony stimulating factor-induced proliferation of TF-1 cells using an assay similar to that described in Example 1E, but with the following modification: For the assay, the cells were washed and TCM-TF-1 medium containing a suboptimal amount of GM-CSF (i.e., 0.4 ng/ml) was added along with the appropriate dilutions of the designated IFN-alpha proteins. The results are shown in Table 8 for feline IFN-alpha proteins expressed as described in Example 7B, lanes labeled Clone #1, Clone #2, Clone #3, Clone #5 and Clone #6, respectively; supernatant from a culture of CHO cells transfected with only the vector described in Example 7B, lane labeled vector; *E. coli*-expressed feline IFN-alpha protein PFeIFN<sub>166e</sub>

produced as described in Example 7D, lane labeled *E.coli*-expressed; and recombinant human IFN-alpha, lane labeled human IFN-alpha. Media alone gave a reading of 128 and recombinant GM-CSF alone gave a reading of 96080.

Table 8. Inhibition of TF-1 cell production by CHO cell-expressed feline IFN-alpha proteins

Dilution	Clone #1	Clone #2	Clone #3	Clone #5	Clone #6	Vector	E. coli expressed	Human IFN alpha
2	15077	7914	21173	15218	13256	53585	19541	559
4	18318	23515	41488	43449	31618	64722	56315	10412
8	22484	25823	48487	40438	43896	83092	80646	21710
16	42138	34274	72145	66266	48775	102423	97255	23585
32	81248	52847	63264	95256				
64	74613	43848	58533	88172	70596	141821	129556	45907
128	59360	48901	48701	54623	90092	155960	151946	40402
256	75788	54017	37391	59849	83022	119491	123794	39299

Table 8 demonstrates that CHO cell-expressed and *E. coli*-expressed feline IFN-alpha subtype proteins inhibited granulocyte-macrophage colony stimulating factor-induced proliferation of TF-1 cells.

#### D. Expression of feline IFN-alpha in *E. coli* and bioactivity thereof

The nucleic acid molecule encoding the mature feline IFN-alpha protein having SEQ ID NO:171 was ligated into the  $\lambda$ cro plasmid vector, using techniques as described in Example 6B, to produce recombinant molecule p $\lambda$ cro-nFeIFNa<sub>498e</sub>. The recombinant molecule was transformed into *E. coli*, using techniques similar to those described in Example 6B to produce recombinant cell *E. coli*:p $\lambda$ cro-nFeIFNa<sub>498e</sub>. The recombinant cell was grown and induced as described in Example 6B. The resulting feline IFN-alpha protein, *E. coli*-expressed PFeIFNa<sub>166e</sub>, which was expressed as an insoluble form, was

solubilized using urea and DTT and refolded using techniques known to those skilled in the art. The refolded *E. coli*-expressed feline IFN-alpha protein PFelIFNa<sub>166e</sub> when tested for antiviral activity as described in Example 7C was found to have significant antiviral activity.

## 5 Example 8

This example describes the isolation and sequencing of feline granulocyte-macrophage colony-stimulating factor (GMCSF) nucleic acid molecules and proteins of the present invention. This example also describes expression of a feline GMCSF protein of the present invention.

10 Nucleic acid molecules encoding feline GMCSF were isolated as follows. A cDNA library was prepared from feline PBMCs stimulated with Con A for 12 hours, as previously described in Example 2. An aliquot of this library was used as a template to amplify feline GMCSF nucleic acid molecules by PCR using Amplitaq DNA polymerase<sup>TM</sup> (PE Applied Biosystems Inc, Foster City, CA) and the following primers and  
 15 conditions. The sequence of the forward primer was 5'CAGGGATCCA CCATGTGGCT GCAGAACCTG CTTTCC 3' (SEQ ID NO:149), and that of the reverse primer was 5' TTACTTCTGG TCTGGTCCCC AGCAGTCAAA GGGGTTGTTA AACAGAAAAT 3' (SEQ ID NO:150). The following PCR protocol was used: one initial denaturation step at 95°C for 5 minutes; then 35 cycles of the following: 94°C for 30 seconds, then  
 20 50°C for 30 seconds, then 72°C for 90 seconds; followed by a final extension at 72°C for 7 minutes. PCR products were cloned into the CMV-Intron A vector and the clones were sequenced as described in Example 7.

A PCR product was isolated, referred to herein as nFeGMCSF<sub>444</sub>, the coding strand of which is represented herein as SEQ ID NO:119, and its complement is denoted SEQ ID NO:121. Translation of the open reading frame in SEQ ID NO:119 suggests that nucleic acid molecule nFeGMCSF<sub>444</sub> encodes a protein containing 144 amino acids, referred to herein as PFeGMCSF<sub>144</sub>, with an amino acid sequence denoted SEQ ID NO:120, assuming an open reading frame in which the first codon spans from nucleotide 10 through nucleotide 12 of SEQ ID NO:119, and the stop codon spans from nucleotide 442 through nucleotide 444 of SEQ ID NO:121. The encoded protein has a predicted molecular weight of 16 kDa. The coding region encoding PFeGMCSF<sub>144</sub> is presented herein as nFeGMCSF<sub>432</sub> which has the nucleotide sequence SEQ ID NO:122 (the coding strand) and SEQ ID NO:123 (the complementary strand). A putative signal peptide cleavage site is between amino acid positions 17 and 18, based on homology with human, mouse and ovine GMCSF proteins. The nucleic acid molecule encoding the proposed mature protein is denoted as nFeGMCSF<sub>381</sub> and has a nucleotide sequence represented herein as SEQ ID NO:124 and a complementary sequence represented herein as SEQ ID NO:126. The amino acid sequence of the putative mature protein, referred to herein as PFeGMCSF<sub>127</sub>, has an amino acid sequence represented herein as SEQ ID NO:125. The number of amino acids in the feline GMCSF protein is the same compared to human, porcine, ovine and canine GMCSF proteins. The feline GMCSF protein is one amino acid longer than bovine GMCSF and three amino acid longer than murine GMCSF.

The deduced amino acid sequence of the full-length feline GMCSF protein of the present invention has four non-conservative changes and one conservative change compared to a GenBank entry for feline GMCSF (accession # AF053007). Amino acids

asparagine, methionine, threonine, and lysine at positions 10, 36, 56 and 126 of the GenBank entry have been changed to glycine, isoleucine, alanine and asparagine, respectively, in PFeGMCSF<sub>144</sub>. PFeGMCSF<sub>144</sub>, containing the above-noted amino acid substitutions, appears to have GMCSF activity, as demonstrated by an experiment in which supernatant collected from Chinese Hamster Ovary (CHO) cells that were transiently transfected with a recombinant molecule encoding a feline GMCSF protein of the present invention was able to induce proliferation of TF-1 cells.

While various embodiments of the present invention have been described in detail, it is apparent that modifications and adaptations of those embodiments will occur to those skilled in the art. It is to be expressly understood, however, that such modifications and adaptations are within the scope of the present invention, as set forth in the following claims.



What is claimed is:

1. An isolated nucleic acid molecule selected from the group consisting of:
  - (a) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and SEQ ID NO:21 or a homolog thereof, wherein said homolog has an at least 50 contiguous nucleotide region identical in sequence to a 50 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and SEQ ID NO:21;
  - (b) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and SEQ ID NO:37, or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a 40 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and SEQ ID NO:37;
  - (c) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and SEQ ID

NO:50, or a homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and  
 5 SEQ ID NO:50;

(d) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and SEQ ID NO:59, or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region  
 10 identical in sequence to a 40 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and SEQ ID NO:59;

(e) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and SEQ ID NO:62, or a  
 15 homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and SEQ ID NO:62;

(f) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID  
 20 NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69 and SEQ ID NO:71, or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid sequence

selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69 and SEQ ID NO:71;

(g) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and SEQ ID NO:79, or a homolog thereof, wherein said homolog has an at least 35 contiguous nucleotide region identical in sequence to a 35 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and SEQ ID NO:79;

(h) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and SEQ ID NO:87, or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and SEQ ID NO:87;

(i) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and SEQ ID NO:106, or a homolog thereof, wherein said homolog has an at least 15 contiguous nucleotide region identical in sequence to a 15 contiguous nucleotide region of a nucleic acid sequence selected from the group

consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and SEQ ID NO:106;

5 (j) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:172; and

(k) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, and SEQ ID NO:126.

2. The nucleic acid molecule of Claim 1,

15 wherein a said nucleic acid molecule as set forth in (a) comprises a nucleic acid sequence that encodes a canine IL-4 protein;

wherein a said nucleic acid molecule as set forth in (b) comprises a nucleic acid sequence that encodes a canine Flt-3 ligand protein;

20 wherein a said nucleic acid molecule as set forth in (c) comprises a nucleic acid sequence that encodes a feline Flt-3 ligand protein;

wherein a said nucleic acid molecule as set forth in (d) comprises a nucleic acid sequence that encodes a canine CD40 protein;

wherein a said nucleic acid molecule as set forth in (e) comprises a nucleic acid sequence that encodes a feline CD40 protein;

wherein a said nucleic acid molecule as set forth in (f) comprises a nucleic acid sequence that encodes a canine CD154 protein;

5        wherein a said nucleic acid molecule as set forth in (g) comprises a nucleic acid sequence that encodes a feline CD154 protein;

wherein a said nucleic acid molecule as set forth in (h) comprises a nucleic acid sequence that encodes a canine IL-5 protein;

10       wherein a said nucleic acid molecule as set forth in (i) comprises a nucleic acid molecule that encodes a canine IL-13 protein;

wherein a said nucleic acid molecule as set forth in (j) consists of a nucleic acid molecule that encodes a feline interferon alpha protein; and

wherein a said nucleic acid molecule as set forth in (k) consists of a nucleic acid molecule that encodes a feline GM-CSF.

15       3.       The nucleic acid molecule of Claim 1,

wherein said nucleic acid molecule of (a) encodes a protein that elicits an immune response against an IL-4 protein having an amino acid sequence selected from the group consisting of SEQ ID NO:2, and SEQ ID NO:20, or a protein that has IL-4 activity;

20       wherein said nucleic acid molecule selected from the group consisting of (b) and (c) encodes a protein that elicits an immune response against a Flt-3 ligand protein having an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:44, and SEQ ID NO:49, or a protein that has Flt-3 ligand activity;

wherein said nucleic acid molecule selected from the group consisting of (d) and (e) encodes a protein that elicits an immune response against a CD40 protein having an amino acid sequence selected from the group consisting of SEQ ID NO:53, SEQ ID NO:58, and SEQ ID NO:61, or a protein that has CD40 activity;

5 wherein said nucleic acid molecule selected from the group consisting of (f) and (g) encodes a protein that elicits an immune response against a CD154 protein having an amino acid sequence selected from the group consisting of SEQ ID NO:65, SEQ ID NO:70, SEQ ID NO:73, and SEQ ID NO:78, or a protein that has CD154 activity;

10 wherein said nucleic acid molecule of (h) encodes a protein that elicits an immune response against an IL-5 protein having an amino acid sequence selected from the group consisting of SEQ ID NO:81 and SEQ ID NO:86, or a protein that has IL-5 activity;

15 wherein said nucleic acid molecule of (i) encodes a protein that elicits an immune response against an IL-13 protein having an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105, or a protein that has IL-13 activity;

20 wherein said nucleic acid molecule of (j) encodes a protein that elicits an immune response against an interferon alpha protein having an amino acid sequence selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and SEQ ID NO:171; and

wherein said nucleic acid molecule of (k) encodes a protein that elicits an immune response against a GM-CSF protein having an amino acid sequence selected from the group consisting of SEQ ID NO:120 and SEQ ID NO:125.

4. The nucleic acid molecule of Claim 1, wherein said nucleic acid molecule comprises a nucleic acid molecule selected from the group consisting of nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, nCaIL-4<sub>324</sub>, nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>, nCaFlt3L<sub>985</sub>, nCaFlt3L<sub>1019</sub>, nCaFlt3L<sub>93</sub>, nCaFlt3L<sub>750</sub>, nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>, nFeFlt3L<sub>873</sub>, nFeFlt3L<sub>795</sub>, nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, nCaCD40<sub>765</sub>, nFeCD40<sub>336</sub>, nCaCD154<sub>390</sub>, nCaCD154<sub>1878</sub>, nCaCD154<sub>780</sub>, nCaCD154<sub>633</sub>, nFeCD154<sub>885</sub>, nFeCD154<sub>780</sub>, nFeCD154<sub>633</sub>, nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, nCaIL-5<sub>345</sub>, nCaIL-13<sub>166</sub>, nCaIL-13<sub>272</sub>, nCaIL-13<sub>278</sub>, nCaIL-13<sub>1302</sub>, nCaIL-13<sub>393</sub>, nCaIL-13<sub>333</sub>, nCaIL-13<sub>1269</sub>, nCaIL-13<sub>390</sub>, nCaIL-13<sub>330</sub>, nFeIFN $\alpha$ <sub>567a</sub>, nFeIFN $\alpha$ <sub>567b</sub>, nFeIFN $\alpha$ <sub>567c</sub>, nFeIFN $\alpha$ <sub>498a</sub>, nFeIFN $\alpha$ <sub>498b</sub>, nFeIFN $\alpha$ <sub>498c</sub>, nFeIFN $\alpha$ <sub>582d</sub>, nFeIFN $\alpha$ <sub>513d</sub>, nFeIFN $\alpha$ <sub>567e</sub>, nFeIFN $\alpha$ <sub>498e</sub>, nFeGMCSF<sub>444</sub>, nFeGMCSF<sub>432</sub>, and nFeGMCSF<sub>381</sub>.

5. The nucleic acid molecule of Claim 1, wherein said nucleic acid molecule is selected from the group consisting of:
- (a) a nucleic acid molecule comprising a nucleic acid sequence that encodes a protein having an amino acid sequence selected from the group consisting of
- (i) SEQ ID NO:2, SEQ ID NO:20, SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:44, SEQ ID NO:49, SEQ ID NO:53, SEQ ID NO:58, SEQ ID NO:61, SEQ ID NO:65, SEQ ID NO:70, SEQ ID NO:73, SEQ ID NO:78, SEQ ID NO:81, SEQ ID NO:86, SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, SEQ ID NO:105, and
- (ii) SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:120, SEQ ID NO:125, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and SEQ ID NO:171; and



(b) a nucleic acid molecule comprising an allelic variant of a nucleic acid molecule encoding a protein having any of said amino acid sequences of group (a) (i).

6. The nucleic acid molecule of Claim 1, wherein said nucleic acid molecule is selected from the group consisting of:

(a) a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of

(i) SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:106, and

(ii) SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124; SEQ ID NO:126, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:172; and

(b) a nucleic acid molecule comprising an allelic variant of a nucleic acid molecule comprising any of said nucleic acid sequences of (a) (i).

7. The nucleic acid molecule of Claim 1, wherein said nucleic acid molecule is an oligonucleotide.

8. A recombinant molecule comprising a nucleic acid molecule as set forth in Claim 1 operatively linked to a transcription control sequence.

9. A recombinant virus comprising a nucleic acid molecule as set forth in Claim 1.

10. A recombinant cell comprising a nucleic acid molecule as set forth in Claim 1.

11. An isolated nucleic acid molecule selected from the group consisting of:
- (a) a nucleic acid molecule having a nucleic acid sequence that is at least about 92 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, and SEQ ID NO:21;
  - (b) a nucleic acid molecule having a nucleic acid sequence that is at least about 75 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and SEQ ID NO:37;
  - (c) a nucleic acid molecule having a nucleic acid sequence that is at least about 75 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and SEQ ID NO:50;
  - (d) a nucleic acid molecule having a nucleic acid sequence that is at least about 70 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and SEQ ID NO:59;
  - (e) a nucleic acid molecule having a nucleic acid sequence that is at least about 70 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and SEQ ID NO:62;

(f) a nucleic acid molecule having a nucleic acid sequence that is at least about 85 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, and SEQ ID NO:71;

5 (g) a nucleic acid molecule having a nucleic acid sequence that is at least about 91 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and SEQ ID NO:79;

(h) a nucleic acid molecule having a nucleic acid sequence that is at least about 90 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and SEQ ID NO:87;

(i) a nucleic acid molecule having a nucleic acid sequence that is at least about 65 percent identical to a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and SEQ ID NO:106;

(j) a nucleic acid molecule having a nucleic acid sequence that is selected from the group consisting of SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID

NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:172; and

- (k) a nucleic acid molecule having a nucleic acid sequence that is selected from the group consisting of SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, and SEQ ID NO:126.

12. An isolated nucleic acid molecule selected from the group consisting of:
- (a) a nucleic acid molecule having a nucleic acid sequence encoding an IL-4 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:20 and (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:20;
  - (b) a nucleic acid molecule having a nucleic acid sequence encoding a Flt-3 ligand protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and SEQ ID NO:34, and (ii) a protein comprising a fragment of at least 25 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and SEQ ID NO:34;
  - (c) a nucleic acid molecule having a nucleic acid sequence encoding a Flt-3 ligand protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:44 and SEQ ID NO:49 and (ii) a protein comprising a fragment of at least 25 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:44 and SEQ ID NO:49;
  - (d) a nucleic acid molecule having a nucleic acid sequence encoding a CD40 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected

from the group consisting of SEQ ID NO:53 and SEQ ID NO:58 and (ii) a protein comprising a fragment of at least 30 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:53 and SEQ ID NO:58;

(e) a nucleic acid molecule having a nucleic acid sequence encoding a  
 5 CD40 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 60 percent identical to an amino acid sequence comprising SEQ ID NO:61 and (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence comprising SEQ ID NO:61;

(f) a nucleic acid molecule having a nucleic acid sequence encoding a  
 10 CD154 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 80 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:65 and SEQ ID NO:70, and (ii) a protein comprising a fragment of at least 35 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:65 and SEQ ID NO:70;

(g) a nucleic acid molecule having a nucleic acid sequence encoding a  
 15 CD154 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:73 and SEQ ID NO:78, and (ii) a protein comprising a fragment of at least 50 amino acids of an amino acid sequence selected from  
 20 the group consisting of SEQ ID NO:73 and SEQ ID NO:78;

(h) a nucleic acid molecule having a nucleic acid sequence encoding an IL-5 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected



from the group consisting of SEQ ID NO:81 and SEQ ID NO:86 and (ii) a protein comprising a fragment of at least 20 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:81 and SEQ ID NO:86;

(i) a nucleic acid molecule having a nucleic acid sequence encoding  
 5 an IL-13 protein selected from the group consisting of (i) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105 and (ii) a protein comprising a fragment of at least 15 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID  
 10 NO:97, SEQ ID NO:100, and SEQ ID NO:105;

(j) a nucleic acid molecule having a nucleic acid sequence encoding an interferon alpha protein having an amino acid sequence that is selected from the group consisting of amino acid sequence SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165,  
 15 SEQ ID NO:168, and SEQ ID NO:171;

(k) a nucleic acid molecule having a nucleic acid sequence encoding a GMCSF protein having an amino acid sequence that is selected from the group consisting of amino acid sequence SEQ ID NO:120, and SEQ ID NO:125; and

(l) a nucleic acid molecule comprising a complement of any of said  
 20 nucleic acid molecules as set forth in (a), (b), (c), (d), (e), (f), (g), (h), (i), (j), or (k),

wherein said IL-4 protein elicits an immune response against an IL-4 protein selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:20 or is a protein with interleukin-4 activity, said Flt-3 ligand protein elicits an immune response against a

Flt-3 ligand protein selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:34, SEQ ID NO:44, and SEQ ID NO:49 or is a protein with Flt-3 ligand activity, said CD40 protein elicits an immune response against a CD40 protein selected from the group consisting of SEQ ID NO:53, SEQ ID NO:58, and SEQ ID NO:61 or is a protein with CD40 activity, said CD154 protein elicits an immune response against a CD154 protein selected from the group consisting of SEQ ID NO:65, SEQ ID NO:70, SEQ ID NO:73, and SEQ ID NO:78 or is a protein with CD154 activity, said IL-5 protein elicits an immune response against a IL-5 protein selected from the group consisting of SEQ ID NO:81 and SEQ ID NO:86 or is a protein with IL-5 activity, said IL-13 protein elicits an immune response against an IL-13 protein selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105 or is a protein with IL-13 activity, said interferon alpha protein elicits an immune response against an interferon alpha protein selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and SEQ ID NO:171 or is a protein with interferon alpha activity, and said GMCSF protein elicits an immune response against a GMCSF protein selected from the group consisting of SEQ ID NO:120 and SEQ ID NO:125 or is a protein with GM-CSF activity.

13. The nucleic acid molecule of Claim 12,
  - wherein said nucleic acid molecule of (a) comprises a nucleic acid sequence that encodes an IL-4 protein;
  - wherein said nucleic acid molecule of (b) comprises a nucleic acid sequence that encodes a Flt-3 ligand protein;

wherein said nucleic acid molecule of (c) comprises a nucleic acid sequence that encodes a Flt-3 ligand protein;

wherein said nucleic acid molecule of (d) comprises a nucleic acid sequence that encodes a CD40 protein;

5            wherein said nucleic acid molecule of (e) comprises a nucleic acid molecule that encodes a CD40 protein;

wherein said nucleic acid molecule of (f) comprises a nucleic acid molecule that encodes a CD154 protein;

10           wherein said nucleic acid molecule of (g) comprises a nucleic acid molecule that encodes a CD154 protein;

wherein said nucleic acid molecule of (h) comprises a nucleic acid molecule that encodes an IL5 protein;

wherein said nucleic acid molecule of (i) comprises a nucleic acid molecule that encodes an IL-13 protein;

15           wherein said nucleic acid molecule of (j) consists of a nucleic acid molecule that encodes an IFN $\alpha$  protein; and

wherein said nucleic acid molecule of (k) consists of a nucleic acid molecule that encodes a GMCSF protein.

14.        The nucleic acid molecule of Claim 12, wherein said nucleic acid  
20        molecule is selected from the group consisting of:

(a)        (i)        a nucleic acid molecule comprising a nucleic acid sequence encoding a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:20; and (ii) a nucleic acid molecule

comprising an allelic variant of a nucleic acid molecule encoding a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:20;

(b) (i) a nucleic acid molecule comprising a nucleic acid sequence encoding a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and SEQ ID NO:34; and (ii) a nucleic acid molecule comprising an allelic variant of a nucleic acid molecule encoding a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and SEQ ID NO:34;

(c) (i) a nucleic acid molecule comprising a nucleic acid sequence encoding a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:44 and SEQ ID NO:49; and (ii) a nucleic acid molecule comprising an allelic variant of a nucleic acid molecule encoding a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:44 and SEQ ID NO:49;

(d) (i) a nucleic acid molecule comprising a nucleic acid sequence encoding a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:53 and SEQ ID NO:58; and (ii) a nucleic acid molecule comprising an allelic variant of a nucleic acid molecule encoding a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:53 and SEQ ID NO:58;

(e) (i) a nucleic acid molecule comprising a nucleic acid sequence encoding a protein comprising an amino acid sequence comprising SEQ ID NO:61; and (ii) a nucleic acid molecule comprising an allelic variant of a nucleic acid molecule encoding a protein having an amino acid sequence comprising SEQ ID NO:61;

5 (f) (i) a nucleic acid molecule comprising a nucleic acid sequence encoding a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:65 and SEQ ID NO:70; and (ii) a nucleic acid molecule comprising an allelic variant of a nucleic acid molecule encoding a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:65 and SEQ ID NO:70;

10 (g) (i) a nucleic acid molecule comprising a nucleic acid sequence encoding a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:73 and SEQ ID NO:78; and (ii) a nucleic acid molecule comprising an allelic variant of a nucleic acid molecule encoding a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:73 and SEQ ID NO:78;

15 (h) (i) a nucleic acid molecule comprising a nucleic acid sequence encoding a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:81 and SEQ ID NO:86; and (ii) a nucleic acid molecule comprising an allelic variant of a nucleic acid molecule encoding a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:81 and SEQ ID  
20 NO:86; and

(i) (i) a nucleic acid molecule comprising a nucleic acid sequence encoding a protein comprising an amino acid sequence selected from the group consisting

of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105; and (ii) a nucleic acid molecule comprising an allelic variant of a nucleic acid molecule encoding a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105.

5           15.     A recombinant molecule comprising a nucleic acid molecule as set forth in Claim 12 operatively linked to a transcription control sequence.

          16.     A recombinant virus comprising a nucleic acid molecule as set forth in Claim 12.

          17.     A recombinant cell comprising a nucleic acid molecule as set forth in  
10    Claim 12.

18. An isolated protein selected from the group consisting of:

- (a) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:4, and SEQ ID NO:19; and
- (ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:20,
- wherein said isolated protein elicits an immune response against a canine IL-4 protein or has IL-4 activity;
- (b) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:9, SEQ ID NO:22, SEQ ID NO:25, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:33, and SEQ ID NO:36; and
- (ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and SEQ ID NO:34,



wherein said isolated protein elicits an immune response against a canine Flt-3 ligand protein or has Flt-3 activity;

(c) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:46, and SEQ ID NO:48; and

(ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:44 and SEQ ID NO:49,

wherein said isolated protein elicits an immune response against a feline Flt-3 ligand protein or has Flt-3 activity;

(d) (i) an isolated protein of at least about 30 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 90 contiguous nucleotide region identical in sequence to a 90 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, and SEQ ID NO:57; and

(ii) an isolated protein of at least about 30 amino acids in length, wherein said protein has an at least 30 contiguous amino acid region identical in sequence to a 30 contiguous amino acid region selected from the group consisting of SEQ ID NO:53, and SEQ ID NO:58,

wherein said isolated protein elicits an immune response against a canine CD40 protein or has CD40 activity;

(e) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence comprising SEQ ID NO:60; and

(ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region comprising SEQ ID NO:61,

wherein said isolated protein elicits an immune response against a feline CD40 protein or has CD40 activity;

(f) (i) an isolated protein of at least about 35 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 105 contiguous nucleotide region identical in sequence to a 105 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, and SEQ ID NO:69; and

(ii) an isolated protein of at least about 35 amino acids in length, wherein said protein has an at least 35 contiguous amino acid region identical in sequence to a 35 contiguous amino acid region selected from the group consisting of SEQ ID NO:65 and SEQ ID NO:70,

wherein said isolated protein elicits an immune response against a canine CD154 protein or has CD154 activity;

(g) (i) an isolated protein of at least about 50 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 150 contiguous nucleotide region identical in sequence to a 150 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:75, and SEQ ID NO:77; and

(ii) an isolated protein of at least about 50 amino acids in length, wherein said protein has an at least 50 contiguous amino acid region identical in sequence to a 50 contiguous amino acid region selected from the group consisting of SEQ ID NO:73 and SEQ ID NO:78, wherein said isolated protein elicits an immune response against a feline CD154 protein or has CD154 activity;

(h) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:83, and SEQ ID NO:85; and

(ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:81 and SEQ ID NO:86,

wherein said isolated protein elicits an immune response against a canine IL-5 protein or has IL-5 activity;

(i) (i) an isolated protein of at least about 15 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, and SEQ ID NO:104; and

(ii) an isolated protein of at least about 15 amino acids in length, wherein said protein has an at least 15 contiguous amino acid region identical in sequence to a 15 contiguous amino acid region selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105,

wherein said isolated protein elicits an immune response against a canine IL-13 protein or has IL-13 activity;

(j) (i) an isolated protein encoded by a nucleic acid molecule selected from the group consisting of SEQ ID NO:107, SEQ ID NO:110, SEQ ID NO:113, SEQ ID NO:116, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:161, SEQ ID NO:164, SEQ ID NO:167, and SEQ ID NO:170, and

(ii) an isolated protein selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and SEQ ID NO:171,

wherein said isolated protein elicits an immune response against a feline interferon alpha protein or has interferon alpha activity;

(k) (i) an isolated protein encoded by a nucleic acid molecule  
selected from the group consisting of SEQ ID NO:119, SEQ ID NO:122, and SEQ ID  
NO:124, and

(ii) an isolated protein selected from the group consisting of  
5 SEQ ID NO:120 and SEQ ID NO:125,

wherein said isolated protein elicits an immune response against a feline GM-CSF  
or has GM-CSF activity.

19. The protein of Claim 18,

wherein said protein of (a) is selected from the group consisting of: (i) an amino  
10 acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:20;  
and (ii) a protein encoded by an allelic variant of a nucleic acid molecule encoding a  
protein selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:20;

wherein said protein of (b) is selected from the group consisting of: (i) an amino  
acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ  
15 ID NO:26, SEQ ID NO:31, and SEQ ID NO:34; and (ii) a protein encoded by an allelic  
variant of a nucleic acid molecule encoding a protein selected from the group consisting  
of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and SEQ ID NO:34;

wherein said protein of (c) is selected from the group consisting of: (i) an amino  
acid sequence selected from the group consisting of SEQ ID NO:44 and SEQ ID NO:49;  
20 and (ii) a protein encoded by an allelic variant of a nucleic acid molecule encoding a  
protein selected from the group consisting of SEQ ID NO:44 and SEQ ID NO:49;

wherein said protein of (d) is selected from the group consisting of: (i) an amino  
acid sequence selected from the group consisting of SEQ ID NO:53 and SEQ ID NO:58;

and (ii) a protein encoded by an allelic variant of a nucleic acid molecule encoding a protein selected from the group consisting of SEQ ID NO:53 and SEQ ID NO:58;

wherein said protein of (e) is selected from the group consisting of: (i) an amino acid sequence comprising SEQ ID NO:61; and a protein encoded by an allelic variant of a nucleic acid molecule encoding the protein SEQ ID NO:61;

wherein said protein of (f) is selected from the group consisting of: (i) an amino acid sequence selected from the group consisting of SEQ ID NO:65 and SEQ ID NO:70; and (ii) a protein encoded by an allelic variant of a nucleic acid molecule encoding a protein selected from the group consisting of SEQ ID NO:65 and SEQ ID NO:70;

wherein said protein of (g) is selected from the group consisting of: (i) an amino acid sequence selected from the group consisting of SEQ ID NO:73 and SEQ ID NO:78; and (ii) a protein encoded by an allelic variant of a nucleic acid molecule encoding a protein selected from the group consisting of SEQ ID NO:73 and SEQ ID NO:78;

wherein said protein of (h) is selected from the group consisting of: (i) an amino acid sequence selected from the group consisting of SEQ ID NO:81 and SEQ ID NO:86; and (ii) a protein encoded by an allelic variant of a nucleic acid molecule encoding a protein selected from the group consisting of SEQ ID NO:81 and SEQ ID NO:86;

wherein said protein of (i) is selected from the group consisting of: (i) SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105; and (ii) a protein encoded by an allelic variant of a nucleic acid molecule encoding a protein selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105;

wherein said protein of (j) is selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and SEQ ID NO:171; and

wherein said protein of (k) is selected from the group consisting of SEQ ID NO:120 and SEQ ID NO:125.

20. An isolated antibody that selectively binds to a protein as set forth in Claim 18.



21. An isolated protein selected from the group consisting of:

- (a) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:20;
- 5 (b) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and SEQ ID NO:34;
- (c) a protein having an amino acid sequence that is at least about 75 percent identical to an amino acid sequence selected from the group consisting of SEQ ID  
10 NO:44 and SEQ ID NO:49;
- (d) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:53 and SEQ ID NO:58;
- (e) a protein having an amino acid sequence that is at least about 60  
15 percent identical to an amino acid sequence comprising SEQ ID NO:61;
- (f) a protein having an amino acid sequence that is at least about 80 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:65 and SEQ ID NO:70;
- (g) a protein having an amino acid sequence that is at least about 85  
20 percent identical to the amino acid sequence SEQ ID NO:73 and SEQ ID NO:78;
- (h) a protein having an amino acid sequence that is at least about 85 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:81 and SEQ ID NO:86;

(i) a protein having an amino acid sequence that is at least about 70 percent identical to an amino acid sequence selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105;

(j) a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and SEQ ID NO:171; and

(k) a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:120, and SEQ ID NO:125.

10            22. An isolated antibody that selectively binds to a protein as set forth in Claim 21.

23. A therapeutic composition that, when administered to an animal, regulates an immune response in said animal, said therapeutic composition comprising a therapeutic compound selected from the group consisting of:

a. an isolated protein comprising an immunoregulatory protein, wherein said protein is selected from the group consisting of

(a) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:4, SEQ ID NO:19; and

(ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:20,

wherein said isolated protein elicits an immune response against a canine IL-4 protein or has IL-4 activity;

(b) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:9, SEQ ID NO:22, SEQ ID NO:25, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:33, and SEQ ID NO:36; and

(ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and SEQ ID NO:34,

5 wherein said isolated protein elicits an immune response against a canine Flt-3 ligand protein or has Flt-3 activity;

(c) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a  
10 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:46, and SEQ ID NO:48; and

(ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in  
15 sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:44 and SEQ ID NO:49,

wherein said isolated protein elicits an immune response against a feline Flt-3 ligand protein or has Flt-3 activity;

(d) (i) an isolated protein of at least about 30 amino acids in  
20 length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 90 contiguous nucleotide region identical in sequence to a 90 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, and SEQ ID NO:57; and

(ii) an isolated protein of at least about 30 amino acids in length, wherein said protein has an at least 30 contiguous amino acid region identical in sequence to a 30 contiguous amino acid region selected from the group consisting of SEQ ID NO:53, SEQ ID NO:58,

5 wherein said isolated protein elicits an immune response against a canine CD40 protein or has CD40 activity;

(e) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a  
10 60 contiguous nucleotide region of a nucleic acid sequence comprising SEQ ID NO:60; and

(ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region comprising the amino acid sequence SEQ  
15 ID NO:61,

wherein said isolated protein elicits an immune response against a feline CD40 protein or has CD40 activity;

(f) (i) an isolated protein of at least about 35 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 105 contiguous nucleotide region identical in sequence to a  
20 105 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, and SEQ ID NO:69; and

(ii) an isolated protein of at least about 35 amino acids in length, wherein said protein has an at least 35 contiguous amino acid region identical in sequence to a 35 contiguous amino acid region selected from the group consisting of SEQ ID NO:65 and SEQ ID NO:70,

5 wherein said isolated protein elicits an immune response against a canine CD154 protein or has CD154 activity;

(g) (i) an isolated protein of at least about 50 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 150 contiguous nucleotide region identical in sequence to a  
10 150 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:75, and SEQ ID NO:77; and

(ii) an isolated protein of at least about 50 amino acids in length, wherein said protein has an at least 50 contiguous amino acid region identical in sequence to a 50 contiguous amino acid region selected from the group consisting of  
15 SEQ ID NO:73 and SEQ ID NO:78,

wherein said isolated protein elicits an immune response against a feline CD154 protein or has CD154 activity;

(h) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a  
20 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:83, and SEQ ID NO:85; and

(ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:81 and SEQ ID NO:86,

5 wherein said isolated protein elicits an immune response against a canine IL-5 protein or has IL-5 activity;

(i) (i) an isolated protein of at least about 15 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 45 contiguous nucleotide region identical in sequence to a  
10 45 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, and SEQ ID NO:104; and

(ii) an isolated protein of at least about 15 amino acids in length, wherein said protein has an at least 15 contiguous amino acid region identical in  
15 sequence to a 15 contiguous amino acid region selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105,

wherein said isolated protein elicits an immune response against a canine IL-13 protein or has IL-13 activity;

(j) (i) an isolated protein encoded by a nucleic acid molecule  
20 selected from the group consisting of SEQ ID NO:107, SEQ ID NO:110, SEQ ID NO:113, SEQ ID NO:116, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:161, SEQ ID NO:164, SEQ ID NO:167, and SEQ ID NO:170, and



(ii) an isolated protein selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156, SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and SEQ ID NO:171,

5 wherein said isolated protein elicits an immune response against a feline interferon alpha protein or has interferon alpha activity; and

(k) (i) an isolated protein encoded by a nucleic acid molecule selected from the group consisting of SEQ ID NO:119, SEQ ID NO:122, and SEQ ID NO:124, and

10 (ii) an isolated protein selected from the group consisting of SEQ ID NO:120 and SEQ ID NO:125,

wherein said isolated protein elicits an immune response against a feline GM-CSF or has GM-CSF activity;

b. a mimotope of any of said immunoregulatory proteins;  
 15 c. a multimeric form of any of said immunoregulatory proteins;  
 d. an isolated nucleic acid molecule selected from the group consisting of

(a) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, SEQ ID NO:21 or a homolog thereof, wherein said  
 20 homolog has an at least 50 contiguous nucleotide region identical in sequence to a 50 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, SEQ ID NO:21;

(b) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and SEQ ID NO:37, or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a 40 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and SEQ ID NO:37;

(c) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and SEQ ID NO:50, or a homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and SEQ ID NO:50;

(d) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and SEQ ID NO:59, or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region

identical in sequence to a 40 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and SEQ ID NO:59;

- (e) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and SEQ ID NO:62, or a homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and SEQ ID NO:62;

- (f) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69 and SEQ ID NO:71, or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69 and SEQ ID NO:71;

- (g) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and SEQ ID NO:79, or a homolog thereof, wherein said homolog has an at least 35 contiguous nucleotide region identical in sequence to a 35 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and SEQ ID NO:79;

(h) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and SEQ ID NO:87, or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, and SEQ ID NO:87;

(i) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and SEQ ID NO:106, or a homolog thereof, wherein said homolog has an at least 15 contiguous nucleotide region identical in sequence to a 15 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and SEQ ID NO:106;

(j) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:107, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID

NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:169, SEQ ID NO:170, and SEQ ID NO:172; and

- (k) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, and SEQ ID NO:126;
  - e. an antibody that selectively binds to any of said immunoregulatory proteins; and
  - f. an inhibitor of a immunoregulatory protein activity identified by its ability to inhibit the activity of any of said immunoregulatory proteins.
- 10        24. The composition of Claim 23, wherein said composition further comprises a component selected from the group consisting of an excipient, an adjuvant and a carrier.
25. The composition of Claim 23, wherein said therapeutic compound is selected from the group consisting of a naked nucleic acid vaccine and a recombinant cell vaccine.

26. A method to regulate an immune response in an animal comprising administering to the animal a therapeutic composition comprising a therapeutic compound selected from the group consisting of:

- (a) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:4, SEQ ID NO:19; and
- (ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:20,  
 wherein said isolated protein elicits an immune response against a canine IL-4 protein or has IL-4 activity;
- (b) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:9, SEQ ID NO:22, SEQ ID NO:25, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:33, and SEQ ID NO:36; and
- (ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in

sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:7, SEQ ID NO:23, SEQ ID NO:26, SEQ ID NO:31, and SEQ ID NO:34,

wherein said isolated protein elicits an immune response against a canine Flt-3 ligand protein or has Flt-3 activity;

5 (c) (i) an isolated protein of at least about 20 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a 60 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:46, and SEQ  
10 ID NO:48; and

(ii) an isolated protein of at least about 20 amino acids in length, wherein said protein has an at least 20 contiguous amino acid region identical in sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:44 and SEQ ID NO:49,

15 wherein said isolated protein elicits an immune response against a feline Flt-3 ligand protein or has Flt-3 activity;

(d) (i) an isolated protein of at least about 30 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 90 contiguous nucleotide region identical in sequence to a  
20 90 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, and SEQ ID NO:57; and

(ii) an isolated protein of at least about 30 amino acids in length, wherein said protein has an at least 30 contiguous amino acid region identical in



sequence to a 30 contiguous amino acid region selected from the group consisting of  
SEQ ID NO:53, SEQ ID NO:58,

wherein said isolated protein elicits an immune response against a canine CD40  
protein or has CD40 activity;

5 (e) (i) an isolated protein of at least about 20 amino acids in  
length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic  
acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a  
60 contiguous nucleotide region of a nucleic acid sequence comprising SEQ ID NO:60;  
and

10 (ii) an isolated protein of at least about 20 amino acids in  
length, wherein said protein has an at least 20 contiguous amino acid region identical in  
sequence to a 20 contiguous amino acid region comprising the amino acid sequence SEQ  
ID NO:61,

wherein said isolated protein elicits an immune response against a feline CD40  
15 protein or has CD40 activity;

(f) (i) an isolated protein of at least about 35 amino acids in  
length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic  
acid molecule has an at least 105 contiguous nucleotide region identical in sequence to a  
105 contiguous nucleotide region of a nucleic acid sequence selected from the group  
20 consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, and SEQ ID NO:69; and

(ii) an isolated protein of at least about 35 amino acids in  
length, wherein said protein has an at least 35 contiguous amino acid region identical in

sequence to a 35 contiguous amino acid region selected from the group consisting of  
SEQ ID NO:65 and SEQ ID NO:70,

wherein said isolated protein elicits an immune response against a canine CD154  
protein or has CD154 activity;

5 (g) (i) an isolated protein of at least about 50 amino acids in  
length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic  
acid molecule has an at least 150 contiguous nucleotide region identical in sequence to a  
150 contiguous nucleotide region of a nucleic acid sequence selected from the group  
consisting of SEQ ID NO:72, SEQ ID NO:75, and SEQ ID NO:77; and

10 (ii) an isolated protein of at least about 50 amino acids in  
length, wherein said protein has an at least 50 contiguous amino acid region identical in  
sequence to a 50 contiguous amino acid region selected from the group consisting of  
SEQ ID NO:73 and SEQ ID NO:78,

wherein said isolated protein elicits an immune response against a feline CD154  
15 protein or has CD154 activity;

(h) (i) an isolated protein of at least about 20 amino acids in  
length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic  
acid molecule has an at least 60 contiguous nucleotide region identical in sequence to a  
60 contiguous nucleotide region of a nucleic acid sequence selected from the group  
20 consisting of SEQ ID NO:80, SEQ ID NO:83, and SEQ ID NO:85; and

(ii) an isolated protein of at least about 20 amino acids in  
length, wherein said protein has an at least 20 contiguous amino acid region identical in

sequence to a 20 contiguous amino acid region selected from the group consisting of SEQ ID NO:81 and SEQ ID NO:86,

wherein said isolated protein elicits an immune response against a canine IL-5 protein or has IL-5 activity;

5                   (i)       (i)       an isolated protein of at least about 15 amino acids in length, wherein said protein is encoded by a nucleic acid molecule, wherein said nucleic acid molecule has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID  
10   NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, and SEQ ID NO:104; and

                  (ii)       an isolated protein of at least about 15 amino acids in length, wherein said protein has an at least 15 contiguous amino acid region identical in sequence to a 15 contiguous amino acid region selected from the group consisting of SEQ ID NO:92, SEQ ID NO:97, SEQ ID NO:100, and SEQ ID NO:105,

15               wherein said isolated protein elicits an immune response against a canine IL-13 protein or has IL-13 activity;

                  (j)       (i)       an isolated protein encoded by a nucleic acid molecule selected from the group consisting of SEQ ID NO:107, SEQ ID NO:110, SEQ ID NO:113, SEQ ID NO:116, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:161, SEQ ID  
20   NO:164, SEQ ID NO:167, and SEQ ID NO:170, and

                  (ii)       an isolated protein selected from the group consisting of SEQ ID NO:108, SEQ ID NO:111, SEQ ID NO:114, SEQ ID NO:117, SEQ ID NO:156,

SEQ ID NO:159, SEQ ID NO:162, SEQ ID NO:165, SEQ ID NO:168, and SEQ ID NO:171,

wherein said isolated protein elicits an immune response against a feline interferon alpha protein or has interferon alpha activity; and

5 (k) (i) an isolated protein encoded by a nucleic acid molecule selected from the group consisting of SEQ ID NO:119, SEQ ID NO:122, and SEQ ID NO:124, and

(ii) an isolated protein selected from the group consisting of SEQ ID NO:120 and SEQ ID NO:125,

10 wherein said isolated protein elicits an immune response against a feline GM-CSF or has GM-CSF activity;

- b. a mimotope of any of said immunoregulatory proteins;
- c. a multimeric form of any of said immunoregulatory proteins;
- d. an isolated nucleic acid molecule selected from the group consisting of

15 (a) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, SEQ ID NO:21 or a homolog thereof, wherein said homolog has an at least 50 contiguous nucleotide region identical in sequence to a 50 contiguous nucleotide region of a nucleic acid sequence selected from the group

20 consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:19, SEQ ID NO:21;

(b) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID

NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and SEQ ID NO:37, or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a 40 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:36, and SEQ ID NO:37;

(c) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and SEQ ID NO:50, or a homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, and SEQ ID NO:50;

(d) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and SEQ ID NO:59, or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a 40 contiguous nucleotide region of a nucleic acid sequence

selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and SEQ ID NO:59;

(e) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and SEQ ID NO:62, or a homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:60 and SEQ ID NO:62;

(f) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69 and SEQ ID NO:71, or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69 and SEQ ID NO:71;

(g) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and SEQ ID NO:79, or a homolog thereof, wherein said homolog has an at least 35 contiguous nucleotide region identical in sequence to a 35 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, and SEQ ID NO:79;

(h) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID

NO:83, SEQ ID NO:84, SEQ ID NO:85, and SEQ ID NO:87, or a homolog thereof,  
 wherein said homolog has an at least 45 contiguous nucleotide region identical in  
 sequence to a 45 contiguous nucleotide region of a nucleic acid sequence selected from  
 the group consisting of SEQ ID NO:80, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84,  
 5 SEQ ID NO:85, and SEQ ID NO:87;

(i) an isolated nucleic acid molecule comprising a nucleic acid  
 sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID  
 NO:90, SEQ ID NO:91, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID  
 NO:96, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID  
 10 NO:103, SEQ ID NO:104, and SEQ ID NO:106, or a homolog thereof, wherein said  
 homolog has an at least 15 contiguous nucleotide region identical in sequence to a 15  
 contiguous nucleotide region of a nucleic acid sequence selected from the group  
 consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID  
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 15 NO:99, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, and SEQ  
 ID NO:106;

(j) an isolated nucleic acid molecule having a nucleic acid sequence  
 selected from the group consisting of SEQ ID NO:107, SEQ ID NO:109, SEQ ID  
 NO:110, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:115, SEQ ID NO:116, SEQ ID  
 20 NO:118, SEQ ID NO:155, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:160, SEQ ID  
 NO:161, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:166, SEQ ID NO:167, SEQ ID  
 NO:169, SEQ ID NO:170 and SEQ ID NO:172; and



(k) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:119, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, and SEQ ID NO:126;

e. an antibody that selectively binds to any of said immunoregulatory proteins; and

f. an inhibitor of a immunoregulatory protein activity identified by its ability to inhibit the activity of any of said immunoregulatory proteins.

27. The method of Claim 26, wherein said animal is selected from the group consisting of canids and felids.

28. The method of Claim 26, wherein said composition further comprises a component selected from the group consisting of an excipient, an adjuvant and a carrier.

29. The method of Claim 26, wherein said protective compound is selected from the group consisting of a naked nucleic acid vaccine and a recombinant cell vaccine.

30. A method to produce an immunoregulatory protein, said method comprising culturing a cell capable of expressing said protein, said protein being encoded by a nucleic acid molecule selected from the group consisting of

(a) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:4, and SEQ ID NO:19, or a homolog thereof, wherein said homolog has an at least 50 contiguous nucleotide region identical in sequence to a 50 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:4, and SEQ ID NO:19;

(b) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:9, SEQ ID NO:22, SEQ ID NO:25, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:33, and SEQ ID NO:36 or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a contiguous nucleotide region of a 40 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:9, SEQ ID NO:22, SEQ ID NO:25, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:33, and SEQ ID NO:36;

(c) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:46, and SEQ ID NO:48, or a homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a contiguous nucleotide region of a 30 contiguous nucleotide region of a nucleic acid sequence selected

from the group consisting of SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:46, and SEQ ID NO:48;

(d) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, and SEQ ID NO:57, or a homolog thereof, wherein said homolog has an at least 40 contiguous nucleotide region identical in sequence to a 40 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:55, and SEQ ID NO:57;

(e) an isolated nucleic acid molecule comprising a nucleic acid sequence comprising SEQ ID NO:60, or a homolog thereof, wherein said homolog has an at least 30 contiguous nucleotide region identical in sequence to a 30 contiguous nucleotide region of a nucleic acid sequence comprising SEQ ID NO:60;

(f) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, and SEQ ID NO:69 or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:67, and SEQ ID NO:69;

(g) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:75, and SEQ ID NO:77 or a homolog thereof, wherein said homolog has an at least 35 contiguous nucleotide region identical in sequence to a 35 contiguous nucleotide region of a nucleic

acid sequence selected from the group consisting of SEQ ID NO:72, SEQ ID NO:75, and SEQ ID NO:77;

(h) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:83, and SEQ ID NO:85, or a homolog thereof, wherein said homolog has an at least 45 contiguous nucleotide region identical in sequence to a 45 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:80, SEQ ID NO:83, and SEQ ID NO:85;

(i) an isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, and SEQ ID NO:104, or a homolog thereof, wherein said homolog has an at least 15 contiguous nucleotide region identical in sequence to a 15 contiguous nucleotide region of a nucleic acid sequence selected from the group consisting of SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:96, SEQ ID NO:99, SEQ ID NO:102, and SEQ ID NO:104;

(j) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:107, SEQ ID NO:110, SEQ ID NO:113, SEQ ID NO:116, SEQ ID NO:155, SEQ ID NO:158, SEQ ID NO:161, SEQ ID NO:164, SEQ ID NO:167, and SEQ ID NO:170; and

(k) an isolated nucleic acid molecule having a nucleic acid sequence selected from the group consisting of SEQ ID NO:119, SEQ ID NO:122, and SEQ ID NO:124.

31. The method of Claim 30, wherein said cell expresses a nucleic acid molecule selected from the group consisting of nCaIL-4<sub>549</sub>, nCaIL-4<sub>396</sub>, nCaIL-4<sub>324</sub>, nCaFlt3L<sub>1013</sub>, nCaFlt3L<sub>882</sub>, nCaFlt3L<sub>804</sub>, nCaFlt3L<sub>828</sub>, nCaFlt3L<sub>985</sub>, nCaFlt3L<sub>1019</sub>, nCaFlt3L<sub>93</sub>, nCaFlt3L<sub>750</sub>, nFeFlt3L<sub>395</sub>, nFeFlt3L<sub>793</sub>, nFeFlt3L<sub>942</sub>, nFeFlt3L<sub>873</sub>, nFeFlt3L<sub>795</sub>,  
5 nCaCD40<sub>321</sub>, nCaCD40<sub>1425</sub>, nCaCD40<sub>822</sub>, nCaCD40<sub>765</sub>, nFeCD40<sub>336</sub>, nCaCD154<sub>390</sub>, nCaCD154<sub>878</sub>, nCaCD154<sub>780</sub>, nCaCD154<sub>633</sub>, nFeCD154<sub>885</sub>, nFeCD154<sub>780</sub>, nFeCD154<sub>633</sub>, nCaIL-5<sub>610</sub>, nCaIL-5<sub>402</sub>, nCaIL-5<sub>345</sub>, nCaIL-13<sub>166</sub>, nCaIL-13<sub>272</sub>, nCaIL-13<sub>278</sub>, nCaIL-13<sub>1302</sub>, nCaIL-13<sub>393</sub>, nCaIL-13<sub>333</sub>, nCaIL-13<sub>1269</sub>, nCaIL-13<sub>390</sub>, nCaIL-13<sub>330</sub>, nFeIFN $\alpha$ <sub>567a</sub>, nFeIFN $\alpha$ <sub>567b</sub>, nFeIFN $\alpha$ <sub>567c</sub>, nFeIFN $\alpha$ <sub>498a</sub>, nFeIFN $\alpha$ <sub>498b</sub>, nFeIFN $\alpha$ <sub>498c</sub>, nFeIFN $\alpha$ <sub>582d</sub>,  
10 nFeIFN $\alpha$ <sub>513d</sub>, nFeIFN $\alpha$ <sub>567e</sub>, nFeIFN $\alpha$ <sub>498e</sub>, nFeGMCSF<sub>444</sub>, nFeGMCSF<sub>432</sub>, and nFeGMCSF<sub>381</sub>.

32. A method to identify a compound capable of regulating an immune response in an animal, said method comprising:

- 5 (a) contacting an isolated canine IL-4 protein with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has T cell proliferation stimulating activity; and determining if said putative inhibitory compound inhibits said activity;
- 10 (b) contacting an isolated canine Flt-3 ligand protein with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has dendritic precursor cell proliferation stimulating activity; and determining if said putative inhibitory compound inhibits said activity;
- 15 (c) contacting an isolated feline Flt-3 ligand protein with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has dendritic precursor cell proliferation stimulating activity; and determining if said putative inhibitory compound inhibits said activity;
- 20 (d) contacting an isolated canine CD40 protein with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has CD40 ligand binding activity; and determining if said putative inhibitory compound inhibits said activity;
- (e) contacting an isolated feline CD40 protein with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has CD40 ligand binding activity; and determining if said putative inhibitory compound inhibits said activity;

(f) contacting an isolated canine CD154 protein with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has B cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity;

5 (g) contacting an isolated feline CD154 protein with a putative inhibitory compound under conditions in which, in the absence of said compound, said protein has B cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity;

(h) contacting an isolated canine IL-5 protein with a putative inhibitory  
10 compound under conditions in which, in the absence of said compound, said protein has TF-1 cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity;

(i) contacting an isolated canine IL-13 protein with a putative  
inhibitory compound under conditions in which, in the absence of said compound, said  
15 protein has TF-1 cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity;

(j) contacting an isolated feline IFN $\alpha$  protein with a putative  
inhibitory compound under conditions in which, in the absence of said compound, said  
protein has inhibition of proliferation of GM-CSF stimulated TF-1 cell activity; and  
20 determining if said putative inhibitory compound inhibits said activity; or

(k) contacting an isolated feline GMCSF protein with a putative  
inhibitory compound under conditions in which, in the absence of said compound, said



protein has TF-1 cell proliferation activity; and determining if said putative inhibitory compound inhibits said activity.

## ABSTRACT

The present invention relates to canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, and/or feline GM-CSF proteins; to canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, and/or feline GM-CSF nucleic acid molecules, including those that encode canine interleukin-4, canine or feline Flt-3 ligand, canine or feline CD40, canine or feline CD154, canine interleukin-5, canine interleukin-13, feline interferon alpha, and/or feline GM-CSF proteins, respectively; to antibodies raised against such proteins; and to inhibitory compounds that regulate such proteins. The present invention also includes methods to identify and obtain such proteins, nucleic acid molecules, antibodies, and inhibitory compounds. Also included in the present invention are therapeutic compositions comprising such proteins, nucleic acid molecules, antibodies and/or inhibitory compounds as well as the use of such therapeutic compositions to regulate an immune response in an animal.

# SEQUENCE LISTING

<110> Sim, Gek-Kee  
Yang, Shumin  
Dreitz, Matthew J.  
Wonderling, Ramani S.

<120> CANINE AND FELINE IMMUNOREGULATORY PROTEINS, NUCLEIC  
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Ala Phe Trp Arg Leu Val Leu Ala Gln Arg Trp Met Val Arg Leu Gln	
75 80 85	
gct gtg gct gga tcc caa atg caa atc ctg ctg gag gct gtc aac acg	343
Ala Val Ala Gly Ser Gln Met Gln Ile Leu Leu Glu Ala Val Asn Thr	
90 95 100	
gag ata cac ttt gtc acc ttc tgt gcc ttc cag ccc ctc ccc agc tgt	391
Glu Ile His Phe Val Thr Phe Cys Ala Phe Gln Pro Leu Pro Ser Cys	
105 110 115	
ctt cgc ttc gtc cag acc aac atc tcc cac ctc ctg cag gac acc tcc	439
Leu Arg Phe Val Gln Thr Asn Ile Ser His Leu Leu Gln Asp Thr Ser	
120 125 130 135	
cag cag ctg gcc gcc ctg aag ccc tgg atc acc cgc agg aat ttc tcc	487
Gln Gln Leu Ala Ala Leu Lys Pro Trp Ile Thr Arg Arg Asn Phe Ser	
140 145 150	
ggg tgc ctg gag ctg cag tgt cag ccc gac tcc tct aca ttg gtg ccc	535
Gly Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Val Pro	
155 160 165	
cca agg agc ccc ggg gcc ctg gag gcc act gcc ttg cca gcc cct cag	583
Pro Arg Ser Pro Gly Ala Leu Glu Ala Thr Ala Leu Pro Ala Pro Gln	
170 175 180	
gca cct cgg ctg ctc ctc ctg ctg ctg ctg ccc gtg gct ctc ctg ctg	631
Ala Pro Arg Leu Leu Leu Leu Leu Leu Leu Pro Val Ala Leu Leu Leu	
185 190 195	



atg tcc act gcc tgg tgc ctg cat tgg cga agg agg cgg cgg cgg agg 679  
 Met Ser Thr Ala Trp Cys Leu His Trp Arg Arg Arg Arg Arg Arg  
 200 205 210 215  
  
 tca ccc tac cct ggg gag cag agg aca ctg agg ccc agc gag cgg agc 727  
 Ser Pro Tyr Pro Gly Glu Gln Arg Thr Leu Arg Pro Ser Glu Arg Ser  
 220 225 230  
  
 cat ctg ccc gag gac aca gag ctg gga cct gga ggg agt cag cta gag 775  
 His Leu Pro Glu Asp Thr Glu Leu Gly Pro Gly Gly Ser Gln Leu Glu  
 235 240 245  
  
 act ggt ccc ttc ctc gac cac gca gcc ccg ctc gct ccc tcc cca gga 823  
 Thr Gly Pro Phe Leu Asp His Ala Ala Pro Leu Ala Pro Ser Pro Gly  
 250 255 260  
  
 tca agg caa cgc ccg ccc cca acg ccc cca aag cca gcc cca gcc cca 871  
 Ser Arg Gln Arg Pro Pro Pro Thr Pro Pro Lys Pro Ala Pro Ala Pro  
 265 270 275  
  
 cct ctc ccc ctc tgt aca aag tcc ttg ccc cca aga aat tgt ata 916  
 Pro Leu Pro Leu Cys Thr Lys Ser Leu Pro Pro Arg Asn Cys Ile  
 280 285 290  
  
 taaatcatcc ttttctacca aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 976  
  
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 1013

<210> 7

<211> 294

<212> PRT

<213> Canis familiaris

<400> 7

Met Ile Val Leu Ala Pro Ala Trp Ser Pro Thr Ala Ser Leu Leu Leu  
 1 5 10 15

Leu Leu Leu Leu Ser Pro Gly Leu Arg Gly Thr Pro Asp Cys Ser Phe  
 20 25 30

Ser His Ser Pro Ile Ser Ser Thr Phe Ala Val Thr Ile Arg Lys Leu  
 35 40 45

Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
 50 55 60

Gln Asp Asp Glu Leu Cys Gly Ala Phe Trp Arg Leu Val Leu Ala Gln  
 65 70 75 80

Arg Trp Met Val Arg Leu Gln Ala Val Ala Gly Ser Gln Met Gln Ile  
 85 90 95

Leu Leu Glu Ala Val Asn Thr Glu Ile His Phe Val Thr Phe Cys Ala  
 100 105 110

Phe Gln Pro Leu Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
 115 120 125

His Leu Leu Gln Asp Thr Ser Gln Gln Leu Ala Ala Leu Lys Pro Trp  
 130 135 140

Ile Thr Arg Arg Asn Phe Ser Gly Cys Leu Glu Leu Gln Cys Gln Pro  
 145 150 155 160

Asp Ser Ser Thr Leu Val Pro Pro Arg Ser Pro Gly Ala Leu Glu Ala  
 165 170 175

Thr Ala Leu Pro Ala Pro Gln Ala Pro Arg Leu Leu Leu Leu Leu Leu  
 180 185 190

Leu Pro Val Ala Leu Leu Leu Met Ser Thr Ala Trp Cys Leu His Trp  
 195 200 205

Arg Arg Arg Arg Arg Arg Arg Ser Pro Tyr Pro Gly Glu Gln Arg Thr  
 210 215 220

Leu Arg Pro Ser Glu Arg Ser His Leu Pro Glu Asp Thr Glu Leu Gly  
 225 230 235 240

Pro Gly Gly Ser Gln Leu Glu Thr Gly Pro Phe Leu Asp His Ala Ala  
 245 250 255

Pro Leu Ala Pro Ser Pro Gly Ser Arg Gln Arg Pro Pro Pro Thr Pro  
 260 265 270

Pro Lys Pro Ala Pro Ala Pro Pro Leu Pro Leu Cys Thr Lys Ser Leu  
 275 280 285

Pro Pro Arg Asn Cys Ile  
 290

<210> 8

<211> 1013

<212> DNA  
<213> Canis familiaris

<400> 8

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tttttttttt ttttttttgg tagaaaagga tgatttatat acaatttctt gggggcaagg 120  
actttgtaca gagggggaga ggtggggctg gggctggctt tgggggcgtt gggggcgggc 180  
gttgccttga tcctggggag ggagcgagcg gggctgcgtg gtcgaggaag ggaccagtct 240  
ctagctgact ccctccaggt ccagctctg tgcctcggg cagatggctc cgctcgttg 300  
gcctcagtgt cctctgctcc ccagggtagg gtgacctcg ccgcccctc ctctgccaat 360  
gcaggcacca ggcagtggac atcagcagga gagccacggg cagcagcagc aggaggagca 420  
gccgaggtgc ctgaggggct ggcaaggcag tggcctccag ggccccggg ctcttgggg 480  
gcaccaatgt agaggagtcg ggctgacact gcagctccag gcacccggag aaattcctgc 540  
gggtgatcca gggcttcagg gcggccagct gctgggaggt gtcctgcagg aggtgggaga 600  
tgttggtctg gacgaagcga agacagctgg ggaggggctg gaaggcacag aaggtgacaa 660  
agtgtatctc cgtgttgaca gcctccagca ggatttgcatt ttgggatcca gccacagcct 720  
ggagccgcac catccagcgc tgggccagga ccaggcgcca gaacgccccg cagagctcgt 780  
cgtcctgcag gttggaggcg acagtgactg gatagtcctg aagcaggtaa tcagacagct 840  
tgcggatggt gaccgcgaag gtggaggaga tggggctgtg gctgaaggag cagtcggggg 900  
tcccgcggag gccggggctg agcagcagca gcagcaacag ggaggcagtt gggctccagg 960  
ctggcgccag cactatcatc tcggccggag gccctcatg cctatgggtca gat 1013

<210> 9  
<211> 882  
<212> DNA  
<213> Canis familiaris

<400> 9

atgatagtgc tggcgccagc ctggagccca actgcctccc tgttgctgct gctgctgctc 60  
agccccggcc tccgcgggac ccccgactgc tccttcagcc acagcccat ctctccacc 120

ttcgcggtca ccatccgcaa gctgtctgat tacctgcttc aggactatcc agtcactgtc 180  
 gcctccaacc tgcaggacga cgagctctgc ggggcgttct ggcgcctggc cctggcccag 240  
 cgctggatgg tgcggctcca ggctgtggct ggatcccaaa tgcaaatcct gctggaggct 300  
 gtcaacacgg agatacactt tgtcaccttc tgtgccttcc agccccctcc cagctgtctt 360  
 cgcttcgtcc agaccaacat ctcccacctc ctgcaggaca cctcccagca gctggccgcc 420  
 ctgaagccct ggatcacccg caggaatttc tccgggtgcc tggagctgca gtgtcagccc 480  
 gactcctcta cattgggtgcc cccaaggagc cccggggccc tggaggccac tgccttgcca 540  
 gcccctcagg cacctcggct gctcctcctg ctgctgctgc ccgtggctct cctgctgatg 600  
 tccactgcct ggtgcctgca ttggcgaagg aggcggcggc ggaggtcacc ctaccctggg 660  
 gagcagagga cactgaggcc cagcgagcgg agccatctgc ccgaggacac agagctggga 720  
 cctggaggga gtcagctaga gactgggtccc ttcctcgacc acgcagcccc gctcgtctcc 780  
 tccccaggat caaggcaacg cccgccccca acgcccccaa agccagcccc agccccacct 840  
 ctccccctct gtacaaagtc cttgccccca agaaattgta ta 882

<210> 10  
 <211> 882  
 <212> DNA  
 <213> Canis familiaris

<400> 10  
 tatacaattt cttgggggca aggactttgt acagaggggg agaggtgggg ctggggctgg 60  
 ctttgggggc gttgggggag ggcgttgctt tgatcctggg gagggagcga gcggggctgc 120  
 gtggtcgagg aagggaaccag tctctagctg actccctcca ggtcccagct ctgtgtcctc 180  
 gggcagatgg ctccgctcgc tgggcctcag tgtcctctgc tccccagggt agggtgacct 240  
 ccgcccgcgc ctcttcgccc aatgcaggca ccaggcagtg gacatcagca ggagagccac 300  
 gggcagcagc agcaggagga gcagccgagg tgcttgaggg gctggcaagg cagtggcctc 360  
 cagggccccg gggctccttg ggggcaccaa tgtagaggag tcgggctgac actgcagctc 420

caggcaccgc gagaaattcc tgcgggtgat ccagggtctc agggcggcca gctgctggga 480  
 ggtgtcctgc aggaggtggg agatgttggg ctggacgaag cgaagacagc tggggagggg 540  
 ctggaaggca cagaaggtga caaagtgtat ctccgtgttg acagcctcca gcaggatttg 600  
 catttgggat ccagccacag cctggagccg caccatccag cgctgggcca ggaccaggcg 660  
 ccagaacgcc ccgcagagct cgtcgtcctg caggttggag gcgacagtga ctggatagtc 720  
 ctgaagcagg taatcagaca gcttgcggtg ggtgaccgcg aaggtggagg agatggggct 780  
 gtggctgaag gagcagtcgg ggggtcccgcg gaggccgggg ctgagcagca gcagcagcaa 840  
 cagggaggca gttgggctcc aggctggcgc cagcactatc at 882

<210> 11

<211> 26

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 11

ctattaatgg gtctcacctc ccaact 26

<210> 12

<211> 24

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 12

tcaactcggg gcacagagtc ttgg 24

<210> 13

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 13

ctggcgccag cctggagccc

20

<210> 14

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 14

gggagatggt ggtctggacg

20

<210> 15

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 15

gaccaggcgc cagaacgc

18

<210> 16

<211> 18

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 16

cggtcaccat ccgcaagc

18

<210> 17

<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 17  
tggcaaggca gtggcctc 18

<210> 18  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 18  
gccgagatga tagtgctggc 20

<210> 19  
<211> 324  
<212> DNA  
<213> Canis familiaris

<220>  
<221> CDS  
<222> (1)..(324)

<400> 19  
cat aac ttc aat att act att aaa gag atc atc aaa atg ttg aac atc 48  
His Asn Phe Asn Ile Thr Ile Lys Glu Ile Ile Lys Met Leu Asn Ile  
1 5 10 15  
  
ctc aca gcg aga aac gac tcg tgc atg gag ctg act gtc aag gac gtc 96  
Leu Thr Ala Arg Asn Asp Ser Cys Met Glu Leu Thr Val Lys Asp Val  
20 25 30  
  
ttc act gct cca aag aac aca agc gat aag gaa atc ttc tgc aga gct 144  
Phe Thr Ala Pro Lys Asn Thr Ser Asp Lys Glu Ile Phe Cys Arg Ala  
35 40 45  
  
gct act gta ctg cgg cag atc tat aca cac aac tgc tcc aac aga tat 192



Ala Thr Val Leu Arg Gln Ile Tyr Thr His Asn Cys Ser Asn Arg Tyr  
 50 55 60

ctc aga gga ctc tac agg aac ctc agc agc atg gca aac aag acc tgt 240  
 Leu Arg Gly Leu Tyr Arg Asn Leu Ser Ser Met Ala Asn Lys Thr Cys  
 65 70 75 80

tct atg aat gaa atc aag aag agt aca ctg aaa gac ttc ttg gaa agg 288  
 Ser Met Asn Glu Ile Lys Lys Ser Thr Leu Lys Asp Phe Leu Glu Arg  
 85 90 95

cta aaa gtg atc atg cag aag aaa tac tac agg cat 324  
 Leu Lys Val Ile Met Gln Lys Lys Tyr Tyr Arg His  
 100 105

<210> 20  
 <211> 108  
 <212> PRT  
 <213> Canis familiaris

<400> 20  
 His Asn Phe Asn Ile Thr Ile Lys Glu Ile Ile Lys Met Leu Asn Ile  
 1 5 10 15

Leu Thr Ala Arg Asn Asp Ser Cys Met Glu Leu Thr Val Lys Asp Val  
 20 25 30

Phe Thr Ala Pro Lys Asn Thr Ser Asp Lys Glu Ile Phe Cys Arg Ala  
 35 40 45

Ala Thr Val Leu Arg Gln Ile Tyr Thr His Asn Cys Ser Asn Arg Tyr  
 50 55 60

Leu Arg Gly Leu Tyr Arg Asn Leu Ser Ser Met Ala Asn Lys Thr Cys  
 65 70 75 80

Ser Met Asn Glu Ile Lys Lys Ser Thr Leu Lys Asp Phe Leu Glu Arg  
 85 90 95

Leu Lys Val Ile Met Gln Lys Lys Tyr Tyr Arg His  
 100 105

<210> 21  
 <211> 324  
 <212> DNA  
 <213> Canis familiaris

<400> 21  
atgcctgtag tattttcttct gcatgatcac ttttagcctt tccaagaagt ctttcagtgt 60  
actcttcttg atttcattca tagaacaggt cttgtttgcc atgctgctga ggttcctgta 120  
gagtcctctg agatatctgt tggagcagtt gtgtgtatag atctgccgca gtacagtagc 180  
agctctgcag aagatttcct tctcgcttgt gttctttgga gcagtgaaga cgtccttgac 240  
agtcagctcc atgcacgagt cgtttctcgc tgtgaggatg ttcaacattt tgatgatctc 300  
tttaatagta atattgaagt tatg 324

<210> 22  
<211> 804  
<212> DNA  
<213> Canis familiaris

<220>  
<221> CDS  
<222> (1)..(804)

<400> 22  
acc ccc gac tgc tcc ttc agc cac agc ccc atc tcc tcc acc ttc gcg 48  
Thr Pro Asp Cys Ser Phe Ser His Ser Pro Ile Ser Ser Thr Phe Ala  
1 5 10 15  
gtc acc atc cgc aag ctg tct gat tac ctg ctt cag gac tat cca gtc 96  
Val Thr Ile Arg Lys Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val  
20 25 30  
act gtc gcc tcc aac ctg cag gac gac gag ctc tgc ggg gcg ttc tgg 144  
Thr Val Ala Ser Asn Leu Gln Asp Asp Glu Leu Cys Gly Ala Phe Trp  
35 40 45  
cgc ctg gtc ctg gcc cag cgc tgg atg gtg cgg ctc cag gct gtg gct 192  
Arg Leu Val Leu Ala Gln Arg Trp Met Val Arg Leu Gln Ala Val Ala  
50 55 60  
gga tcc caa atg caa atc ctg ctg gag gct gtc aac acg gag ata cac 240  
Gly Ser Gln Met Gln Ile Leu Leu Glu Ala Val Asn Thr Glu Ile His  
65 70 75 80  
ttt gtc acc ttc tgt gcc ttc cag ccc ctc ccc agc tgt ctt cgc ttc 288  
Phe Val Thr Phe Cys Ala Phe Gln Pro Leu Pro Ser Cys Leu Arg Phe  
85 90 95

gtc cag acc aac atc tcc cac ctc ctg cag gac acc tcc cag cag ctg	336
Val Gln Thr Asn Ile Ser His Leu Leu Gln Asp Thr Ser Gln Gln Leu	
100 105 110	
gcc gcc ctg aag ccc tgg atc acc cgc agg aat ttc tcc ggg tgc ctg	384
Ala Ala Leu Lys Pro Trp Ile Thr Arg Arg Asn Phe Ser Gly Cys Leu	
115 120 125	
gag ctg cag tgt cag ccc gac tcc tct aca ttg gtg ccc cca agg agc	432
Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Val Pro Pro Arg Ser	
130 135 140	
ccc ggg gcc ctg gag gcc act gcc ttg cca gcc cct cag gca cct cgg	480
Pro Gly Ala Leu Glu Ala Thr Ala Leu Pro Ala Pro Gln Ala Pro Arg	
145 150 155 160	
ctg ctc ctc ctg ctg ctg ctg ccc gtg gct ctc ctg ctg atg tcc act	528
Leu Leu Leu Leu Leu Leu Leu Pro Val Ala Leu Leu Leu Met Ser Thr	
165 170 175	
gcc tgg tgc ctg cat tgg cga agg agg cgg cgg cgg agg tca ccc tac	576
Ala Trp Cys Leu His Trp Arg Arg Arg Arg Arg Arg Arg Ser Pro Tyr	
180 185 190	
cct ggg gag cag agg aca ctg agg ccc agc gag cgg agc cat ctg ccc	624
Pro Gly Glu Gln Arg Thr Leu Arg Pro Ser Glu Arg Ser His Leu Pro	
195 200 205	
gag gac aca gag ctg gga cct gga ggg agt cag cta gag act ggt ccc	672
Glu Asp Thr Glu Leu Gly Pro Gly Gly Ser Gln Leu Glu Thr Gly Pro	
210 215 220	
ttc ctc gac cac gca gcc ccg ctc gct ccc tcc cca gga tca agg caa	720
Phe Leu Asp His Ala Ala Pro Leu Ala Pro Ser Pro Gly Ser Arg Gln	
225 230 235 240	
cgc ccg ccc cca acg ccc cca aag cca gcc cca gcc cca cct ctc ccc	768
Arg Pro Pro Pro Thr Pro Pro Lys Pro Ala Pro Ala Pro Pro Leu Pro	
245 250 255	
ctc tgt aca aag tcc ttg ccc cca aga aat tgt ata	804
Leu Cys Thr Lys Ser Leu Pro Pro Arg Asn Cys Ile	
260 265	

<210> 23

<211> 268

<212> PRT

<213> Canis familiaris

<400> 23

Thr Pro Asp Cys Ser Phe Ser His Ser Pro Ile Ser Ser Thr Phe Ala  
1 5 10 15

Val Thr Ile Arg Lys Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val  
20 25 30

Thr Val Ala Ser Asn Leu Gln Asp Asp Glu Leu Cys Gly Ala Phe Trp  
35 40 45

Arg Leu Val Leu Ala Gln Arg Trp Met Val Arg Leu Gln Ala Val Ala  
50 55 60

Gly Ser Gln Met Gln Ile Leu Leu Glu Ala Val Asn Thr Glu Ile His  
65 70 75 80

Phe Val Thr Phe Cys Ala Phe Gln Pro Leu Pro Ser Cys Leu Arg Phe  
85 90 95

Val Gln Thr Asn Ile Ser His Leu Leu Gln Asp Thr Ser Gln Gln Leu  
100 105 110

Ala Ala Leu Lys Pro Trp Ile Thr Arg Arg Asn Phe Ser Gly Cys Leu  
115 120 125

Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Leu Val Pro Pro Arg Ser  
130 135 140

Pro Gly Ala Leu Glu Ala Thr Ala Leu Pro Ala Pro Gln Ala Pro Arg  
145 150 155 160

Leu Leu Leu Leu Leu Leu Leu Pro Val Ala Leu Leu Leu Met Ser Thr  
165 170 175

Ala Trp Cys Leu His Trp Arg Arg Arg Arg Arg Arg Ser Pro Tyr  
180 185 190

Pro Gly Glu Gln Arg Thr Leu Arg Pro Ser Glu Arg Ser His Leu Pro  
195 200 205

Glu Asp Thr Glu Leu Gly Pro Gly Gly Ser Gln Leu Glu Thr Gly Pro  
210 215 220

Phe Leu Asp His Ala Ala Pro Leu Ala Pro Ser Pro Gly Ser Arg Gln  
225 230 235 240

Arg Pro Pro Pro Thr Pro Pro Lys Pro Ala Pro Ala Pro Pro Leu Pro  
 245 250 255

Leu Cys Thr Lys Ser Leu Pro Pro Arg Asn Cys Ile  
 260 265

<210> 24

<211> 804

<212> DNA

<213> Canis familiaris

<400> 24

tatacaattt cttgggggca aggactttgt acagaggggg agaggtgggg ctggggctgg 60  
 ctttgggggc gttgggggcg ggcgttgctt tgatcctggg gagggagcga gcggggctgc 120  
 gtggtcgagg aagggaccag tctctagctg actccctcca ggtcccagct ctgtgtcctc 180  
 gggcagatgg ctccgctcgc tgggcctcag tgtcctctgc tccccagggt agggtgacct 240  
 ccgccgccgc ctcttctgcc aatgcaggca ccaggcagtg gacatcagca ggagagccac 300  
 gggcagcagc agcaggagga gcagccgagg tgcctgaggg gctggcaagg cagtggcctc 360  
 cagggccccc gggctccttg ggggcaccaa tgtagaggag tcgggctgac actgcagctc 420  
 caggcacccg gagaaattcc tgcgggtgat ccagggcttc agggcggcca gctgctggga 480  
 ggtgtcctgc aggaggtggg agatgttggt ctggacgaag cgaagacagc tggggagggg 540  
 ctggaaggca cagaaggatga caaagtgtat ctccgtgttg acagcctcca gcaggatttg 600  
 catttgggat ccagccacag cctggagccg caccatccag cgctgggcca ggaccaggcg 660  
 ccagaacgcc ccgcagagct cgtcgtcctg caggttggag gcgacagtga ctggatagtc 720  
 ctgaagcagg taatcagaca gcttgccgat ggtgaccgcg aagggtggagg agatggggct 780  
 gtggctgaag gagcagtcgg gggt 804

<210> 25

<211> 985

<212> DNA

<213> Canis familiaris

<220>

<221> CDS

<222> (74)..(901)

<400> 25

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gcctccggcc gag atg ata gtg ctg gcg cca gcc tgg agc cca act gcc 109  
Met Ile Val Leu Ala Pro Ala Trp Ser Pro Thr Ala  
1 5 10

tcc ctg ttg ctg ctg ctg ctg ctc agc ccc ggc ctc cgc ggg acc ccc 157  
Ser Leu Leu Leu Leu Leu Leu Leu Ser Pro Gly Leu Arg Gly Thr Pro  
15 20 25

gac tgc tcc ttc agc cac agc ccc atc tcc tcc acc ttc gcg gtc acc 205  
Asp Cys Ser Phe Ser His Ser Pro Ile Ser Ser Thr Phe Ala Val Thr  
30 35 40

atc cgc aag ctg tct gat tac ctg ctt cag gac tat cca gtc act gtc 253  
Ile Arg Lys Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val  
45 50 55 60

gcc tcc aac ctg cag gac gac gag ctc tgc ggg gcg ttc tgg cgc ctg 301  
Ala Ser Asn Leu Gln Asp Asp Glu Leu Cys Gly Ala Phe Trp Arg Leu  
65 70 75

gtc ctg gcc cag cgc tgg atg gtg cgg ctc cag gct gtg gct gga tcc 349  
Val Leu Ala Gln Arg Trp Met Val Arg Leu Gln Ala Val Ala Gly Ser  
80 85 90

caa atg caa atc ctg ctg gag gct gtc aac acg gag ata cac ttt gtc 397  
Gln Met Gln Ile Leu Leu Glu Ala Val Asn Thr Glu Ile His Phe Val  
95 100 105

acc ttc tgt gcc ttc cag gac acc tcc cag cag ctg gcc gcc ctg aag 445  
Thr Phe Cys Ala Phe Gln Asp Thr Ser Gln Gln Leu Ala Ala Leu Lys  
110 115 120

ccc tgg atc acc cgc agg aat ttc tcc ggg tgc ctg gag ctg cag tgt 493  
Pro Trp Ile Thr Arg Arg Asn Phe Ser Gly Cys Leu Glu Leu Gln Cys  
125 130 135 140

cag ccc gac tcc tct aca ttg gtg ccc cca agg agc ccc ggg gcc ctg 541  
Gln Pro Asp Ser Ser Thr Leu Val Pro Pro Arg Ser Pro Gly Ala Leu  
145 150 155

gag gcc act gcc ttg cca gcc cct cag gca cct cgg ctg ctc ctc ctg 589

Glu	Ala	Thr	Ala	Leu	Pro	Ala	Pro	Gln	Ala	Pro	Arg	Leu	Leu	Leu	Leu	
			160					165				170				
ctg	ctg	ctg	ccc	gtg	gct	ctc	ctg	ctg	atg	tcc	act	gcc	tgg	tgc	ctg	637
Leu	Leu	Leu	Pro	Val	Ala	Leu	Leu	Leu	Met	Ser	Thr	Ala	Trp	Cys	Leu	
			175					180				185				
cat	tgg	cga	agg	agg	cgg	cgg	cgg	agg	tca	ccc	tac	cct	ggg	gag	cag	685
His	Trp	Arg	Arg	Arg	Arg	Arg	Arg	Arg	Ser	Pro	Tyr	Pro	Gly	Glu	Gln	
	190							195			200					
agg	aca	ctg	agg	ccc	agc	gag	cgg	agc	cat	ctg	ccc	gag	gac	aca	gag	733
Arg	Thr	Leu	Arg	Pro	Ser	Glu	Arg	Ser	His	Leu	Pro	Glu	Asp	Thr	Glu	
205						210				215					220	
ctg	gga	cct	gga	ggg	agt	cag	cta	gag	act	ggt	ccc	ttc	ctc	gac	cac	781
Leu	Gly	Pro	Gly	Gly	Ser	Gln	Leu	Glu	Thr	Gly	Pro	Phe	Leu	Asp	His	
				225					230					235		
gca	gcc	ccg	ctc	gct	ccc	tcc	cca	gga	tca	agg	caa	cgc	ccg	ccc	cca	829
Ala	Ala	Pro	Leu	Ala	Pro	Ser	Pro	Gly	Ser	Arg	Gln	Arg	Pro	Pro	Pro	
			240					245				250				
acg	ccc	cca	aag	cca	gcc	cca	gcc	cca	cct	ctc	ccc	ctc	tgt	aca	aag	877
Thr	Pro	Pro	Lys	Pro	Ala	Pro	Ala	Pro	Pro	Leu	Pro	Leu	Cys	Thr	Lys	
		255					260					265				
tcc	ttg	ccc	cca	aga	aat	tgt	ata	taa	tcatcc	ttttctacca	gcaaaaaaaaa					931
Ser	Leu	Pro	Pro	Arg	Asn	Cys	Ile									
	270					275										
aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaa									985

<210> 26  
 <211> 276  
 <212> PRT  
 <213> Canis familiaris

<400> 26  
 Met Ile Val Leu Ala Pro Ala Trp Ser Pro Thr Ala Ser Leu Leu Leu  
 1 5 10 15  
 Leu Leu Leu Leu Ser Pro Gly Leu Arg Gly Thr Pro Asp Cys Ser Phe  
 20 25 30  
 Ser His Ser Pro Ile Ser Ser Thr Phe Ala Val Thr Ile Arg Lys Leu  
 35 40 45



Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
50 55 60

Gln Asp Asp Glu Leu Cys Gly Ala Phe Trp Arg Leu Val Leu Ala Gln  
65 70 75 80

Arg Trp Met Val Arg Leu Gln Ala Val Ala Gly Ser Gln Met Gln Ile  
85 90 95

Leu Leu Glu Ala Val Asn Thr Glu Ile His Phe Val Thr Phe Cys Ala  
100 105 110

Phe Gln Asp Thr Ser Gln Gln Leu Ala Ala Leu Lys Pro Trp Ile Thr  
115 120 125

Arg Arg Asn Phe Ser Gly Cys Leu Glu Leu Gln Cys Gln Pro Asp Ser  
130 135 140

Ser Thr Leu Val Pro Pro Arg Ser Pro Gly Ala Leu Glu Ala Thr Ala  
145 150 155 160

Leu Pro Ala Pro Gln Ala Pro Arg Leu Leu Leu Leu Leu Leu Leu Pro  
165 170 175

Val Ala Leu Leu Leu Met Ser Thr Ala Trp Cys Leu His Trp Arg Arg  
180 185 190

Arg Arg Arg Arg Arg Ser Pro Tyr Pro Gly Glu Gln Arg Thr Leu Arg  
195 200 205

Pro Ser Glu Arg Ser His Leu Pro Glu Asp Thr Glu Leu Gly Pro Gly  
210 215 220

Gly Ser Gln Leu Glu Thr Gly Pro Phe Leu Asp His Ala Ala Pro Leu  
225 230 235 240

Ala Pro Ser Pro Gly Ser Arg Gln Arg Pro Pro Pro Thr Pro Pro Lys  
245 250 255

Pro Ala Pro Ala Pro Pro Leu Pro Leu Cys Thr Lys Ser Leu Pro Pro  
260 265 270

Arg Asn Cys Ile  
275

<210> 27

<211> 985  
<212> DNA  
<213> Canis familiaris

<400> 27

tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60  
  
ttgctggtag aaaaggatga tttatataca atttcttggg ggcaaggact ttgtacagag 120  
  
ggggagaggt ggggctgggg ctggccttgg gggcgttggg ggcgggcggt gccttgatcc 180  
  
tggggagggg gcgagcgggg ctgcgtggtc gaggaaggga ccagtctcta gctgactccc 240  
  
tccaggtccc agctctgtgt cctcgggcag atggctccgc tcgctgggccc tcagtgtcct 300  
  
ctgctcccca gggtaggggtg acctccgccg ccgcctcctt cgccaatgca ggcaccaggc 360  
  
agtggacatc agcaggagag ccacgggcag cagcagcagg aggagcagcc gaggtgcctg 420  
  
aggggctggc aaggcagtgg cctccagggc cccggggctc cttgggggca ccaatgtaga 480  
  
ggagtcgggc tgacactgca gctccaggca cccggagaaa ttcctgcggg tgatccaggg 540  
  
cttcagggcg gccagctgct gggaggtgtc ctggaaggca cagaagggtga caaagtgtat 600  
  
ctccgtgttg acagcctcca gcaggatttg catttgggat ccagccacag cctggagccg 660  
  
caccatccag cgctgggcca ggaccaggcg ccagaacgcc ccgcagagct cgtcgtcctg 720  
  
caggttggag gcgacagtga ctggatagtc ctgaagcagg taatcagaca gcttgcggat 780  
  
ggtgaccgcg aaggtggagg agatggggct gtggctgaag gagcagtcgg ggggtcccgcg 840  
  
gaggccgggg ctgagcagca gcagcagcaa cagggaggca gttgggctcc aggctggcgc 900  
  
cagcactatc atctcggccg gaggcccctc atgcctatgg tcagatcagg cttgccccag 960  
  
ctgggcgtgg aaggggccag gccgg 985

<210> 28  
<211> 828  
<212> DNA  
<213> Canis familiaris

<400> 28

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agccccggcc tccgcgggac ccccgactgc tccttcagcc acagccccat ctctccacc 120  
 ttgcggttca ccatccgcaa gctgtctgat tacctgcttc aggactatcc agtcactgtc 180  
 gcctccaacc tgcaggacga cgagctctgc ggggcgttct ggcgcctggc cctggcccag 240  
 cgctggatgg tgcggctcca ggctgtggct ggatcccaaa tgcaaatact gctggaggct 300  
 gtcaacacgg agatacactt tgtcaccttc tgtgccttcc aggacacctc ccagcagctg 360  
 gccgccctga agccctggat caccgcagc aatttctccg ggtgcctgga gctgcagtgt 420  
 cagcccgact cctctacatt ggtgccccca aggagccccg gggccctgga ggccactgcc 480  
 ttgccagccc ctccaggacc tcggctgctc ctctgctgc tgctgcccggt ggctctcctg 540  
 ctgatgtcca ctgcctgggtg cctgcattgg cgaaggaggc ggcggcggag gtcaccctac 600  
 cctgggggagc agaggacact gaggcccagc gagcggagcc atctgcccga ggacacagag 660  
 ctgggacctg gagggagtca gctagagact ggtcccttcc tcgaccacgc agccccgctc 720  
 gctccctccc caggatcaag gcaacgcccc cccccaacgc ccccaaagcc agccccagcc 780  
 ccacctctcc ccctctgtac aaagtccttg cccccaagaa attgtata 828

<210> 29  
 <211> 828  
 <212> DNA  
 <213> Canis familiaris

<400> 29  
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 ctttgggggc gttgggggag ggcgttgctt tgatcctggg gagggagcga gcggggctgc 120  
 gtggtcagag aagggaccag tctctagctg actccctcca ggtcccagct ctgtgtcctc 180  
 gggcagatgg ctccgctcgc tgggcctcag tgtcctctgc tccccagggt agggtgacct 240  
 ccgccgccgc ctcttcgccc aatgcaggca ccaggcagtg gacatcagca ggagagccac 300  
 gggcagcagc agcaggagga gcagccgagg tgcttgaggg gctggcaagg cagtggcctc 360  
 cagggccccg gggctccttg ggggcaccaa thtagaggag tcgggctgac actgcagctc 420  
 caggcacccg gagaaattcc tgcgggtgat ccagggcttc agggcggcca gctgctggga 480

ggtgtcctgg aaggcacaga aggtgacaaa gtgtatctcc gtgttgacag cctccagcag 540  
 gatttgcat tgggatccag ccacagcctg gagccgcacc atccagcgct gggccaggac 600  
 caggcgccag aacgccccgc agagctcgtc gtctgcagg ttggaggcga cagtgactgg 660  
 atagtcctga agcaggtaat cagacagctt gcggatgggtg accgcgaagg tggaggagat 720  
 ggggctgtgg ctgaaggagc agtcgggggt cccgcggagg ccggggctga gcagcagcag 780  
 cagcaacagg gaggcagttg ggctccaggc tggcgccagc actatcat 828

<210> 30  
 <211> 750  
 <212> DNA  
 <213> Canis familiaris

<220>  
 <221> CDS  
 <222> (1)..(750)

<400> 30  
 acc ccc gac tgc tcc ttc agc cac agc ccc atc tcc tcc acc ttc gcg 48  
 Thr Pro Asp Cys Ser Phe Ser His Ser Pro Ile Ser Ser Thr Phe Ala  
 1 5 10 15  
 gtc acc atc cgc aag ctg tct gat tac ctg ctt cag gac tat cca gtc 96  
 Val Thr Ile Arg Lys Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val  
 20 25 30  
 act gtc gcc tcc aac ctg cag gac gac gag ctc tgc ggg gcg ttc tgg 144  
 Thr Val Ala Ser Asn Leu Gln Asp Asp Glu Leu Cys Gly Ala Phe Trp  
 35 40 45  
 cgc ctg gtc ctg gcc cag cgc tgg atg gtg cgg ctc cag gct gtg gct 192  
 Arg Leu Val Leu Ala Gln Arg Trp Met Val Arg Leu Gln Ala Val Ala  
 50 55 60  
 gga tcc caa atg caa atc ctg ctg gag gct gtc aac acg gag ata cac 240  
 Gly Ser Gln Met Gln Ile Leu Leu Glu Ala Val Asn Thr Glu Ile His  
 65 70 75 80  
 ttt gtc acc ttc tgt gcc ttc cag gac acc tcc cag cag ctg gcc gcc 288  
 Phe Val Thr Phe Cys Ala Phe Gln Asp Thr Ser Gln Gln Leu Ala Ala  
 85 90 95

ctg aag ccc tgg atc acc cgc agg aat ttc tcc ggg tgc ctg gag ctg	336
Leu Lys Pro Trp Ile Thr Arg Arg Asn Phe Ser Gly Cys Leu Glu Leu	
100 105 110	
cag tgt cag ccc gac tcc tct aca ttg gtg ccc cca agg agc ccc ggg	384
Gln Cys Gln Pro Asp Ser Ser Thr Leu Val Pro Pro Arg Ser Pro Gly	
115 120 125	
gcc ctg gag gcc act gcc ttg cca gcc cct cag gca cct cgg ctg ctc	432
Ala Leu Glu Ala Thr Ala Leu Pro Ala Pro Gln Ala Pro Arg Leu Leu	
130 135 140	
ctc ctg ctg ctg ctg ccc gtg gct ctc ctg ctg atg tcc act gcc tgg	480
Leu Leu Leu Leu Leu Pro Val Ala Leu Leu Leu Met Ser Thr Ala Trp	
145 150 155 160	
tgc ctg cat tgg cga agg agg cgg cgg cgg agg tca ccc tac cct ggg	528
Cys Leu His Trp Arg Arg Arg Arg Arg Arg Ser Pro Tyr Pro Gly	
165 170 175	
gag cag agg aca ctg agg ccc agc gag cgg agc cat ctg ccc gag gac	576
Glu Gln Arg Thr Leu Arg Pro Ser Glu Arg Ser His Leu Pro Glu Asp	
180 185 190	
aca gag ctg gga cct gga ggg agt cag cta gag act ggt ccc ttc ctc	624
Thr Glu Leu Gly Pro Gly Gly Ser Gln Leu Glu Thr Gly Pro Phe Leu	
195 200 205	
gac cac gca gcc ccg ctc gct ccc tcc cca gga tca agg caa cgc ccg	672
Asp His Ala Ala Pro Leu Ala Pro Ser Pro Gly Ser Arg Gln Arg Pro	
210 215 220	
ccc cca acg ccc cca aag cca gcc cca gcc cca cct ctc ccc ctc tgt	720
Pro Pro Thr Pro Pro Lys Pro Ala Pro Ala Pro Pro Leu Pro Leu Cys	
225 230 235 240	
aca aag tcc ttg ccc cca aga aat tgt ata	750
Thr Lys Ser Leu Pro Pro Arg Asn Cys Ile	
245 250	

<210> 31  
 <211> 250  
 <212> PRT  
 <213> Canis familiaris

<400> 31  
 Thr Pro Asp Cys Ser Phe Ser His Ser Pro Ile Ser Ser Thr Phe Ala

1	5	10	15
Val Thr Ile Arg Lys Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val			
	20	25	30
Thr Val Ala Ser Asn Leu Gln Asp Asp Glu Leu Cys Gly Ala Phe Trp			
	35	40	45
Arg Leu Val Leu Ala Gln Arg Trp Met Val Arg Leu Gln Ala Val Ala			
	50	55	60
Gly Ser Gln Met Gln Ile Leu Leu Glu Ala Val Asn Thr Glu Ile His			
	65	70	75
Phe Val Thr Phe Cys Ala Phe Gln Asp Thr Ser Gln Gln Leu Ala Ala			
	85	90	95
Leu Lys Pro Trp Ile Thr Arg Arg Asn Phe Ser Gly Cys Leu Glu Leu			
	100	105	110
Gln Cys Gln Pro Asp Ser Ser Thr Leu Val Pro Pro Arg Ser Pro Gly			
	115	120	125
Ala Leu Glu Ala Thr Ala Leu Pro Ala Pro Gln Ala Pro Arg Leu Leu			
	130	135	140
Leu Leu Leu Leu Leu Pro Val Ala Leu Leu Leu Met Ser Thr Ala Trp			
	145	150	155
Cys Leu His Trp Arg Arg Arg Arg Arg Arg Arg Ser Pro Tyr Pro Gly			
	165	170	175
Glu Gln Arg Thr Leu Arg Pro Ser Glu Arg Ser His Leu Pro Glu Asp			
	180	185	190
Thr Glu Leu Gly Pro Gly Gly Ser Gln Leu Glu Thr Gly Pro Phe Leu			
	195	200	205
Asp His Ala Ala Pro Leu Ala Pro Ser Pro Gly Ser Arg Gln Arg Pro			
	210	215	220
Pro Pro Thr Pro Pro Lys Pro Ala Pro Ala Pro Pro Leu Pro Leu Cys			
	225	230	235
Thr Lys Ser Leu Pro Pro Arg Asn Cys Ile			
	245	250	

<210> 32  
 <211> 750  
 <212> DNA  
 <213> Canis familiaris

<400> 32  
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 gtggtcgagg aagggaccag tctctagctg actccctcca ggtcccagct ctgtgtcctc 180  
 gggcagatgg ctccgctcgc tgggcctcag tgtcctctgc tccccagggg agggtgacct 240  
 ccgccgccgc ctcccttcgcc aatgcaggca ccaggcagtg gacatcagca ggagagccac 300  
 gggcagcagc agcaggagga gcagccgagg tgcctgaggg gctggcaagg cagtggcctc 360  
 cagggccccg gggctccttg ggggcaccaa tgtagaggag tcgggctgac actgcagctc 420  
 caggcacccg gagaaattcc tgcgggtgat ccagggcttc agggcggcca gctgctggga 480  
 ggtgtcctgg aaggcacaga aggtgacaaa gtgtatctcc gtgttgacag cctccagcag 540  
 gatttgcatt tgggatccag ccacagcctg gagccgcacc atccagcgct gggccaggac 600  
 caggcgccag aacgccccgc agagctcgtc gtcctgcagg ttggaggcga cagtgactgg 660  
 atagtcttga agcaggtaat cagacagctt gcggatgggt accgcgaagg tggaggagat 720  
 ggggctgtgg ctgaaggagc agtcgggggt 750

<210> 33  
 <211> 1019  
 <212> DNA  
 <213> Canis familiaris

<220>  
 <221> CDS  
 <222> (74)..(166)

<400> 33  
 ccggcctggc cccttccacg cccagctggg gcaagcctga tctgaccata ggcatgaggg 60  
 gcctccggcc gag atg ata gtg ctg gcg cca gcc tgg agc cca act gtg 109  
 Met Ile Val Leu Ala Pro Ala Trp Ser Pro Thr Val  
 1 5 10



cgt ata ccc ggg gga caa ggc ggg gga cag gca gag cgc tac cga gct 157  
 Arg Ile Pro Gly Gly Gln Gly Gly Gly Gln Ala Glu Arg Tyr Arg Ala  
           15                          20                          25

ggg cag agc tgagagagca gacggacaga ggccctccctg ttgctgctgc 206  
 Gly Gln Ser  
           30

tgctgctcag ccccgccctc cgcgggaccc ccgactgctc cttcagccac agccccatct 266  
 cctccacctt cgcggtcacc atccgcaagc tgtctgatta cctgcttcag gactatccag 326  
 tcaactgtcg ctccaacctg caggacgacg agctctgcgg ggcgttctgg cgcctgggtcc 386  
 tggcccagcg ctggatgggtg cggctccagg ctgtggctgg atcccaaag caaatcctgc 446  
 tggaggctgt caacacggag atacactttg tcaccttctg tgccttcag gacacctccc 506  
 agcagctggc cgccctgaag ccctggatca cccgcaggaa tttctccggg tgcctggagc 566  
 tgcagtgtca gcccgactcc tctacattgg tgccccaag gagccccggg gccctggagg 626  
 ccactgcctt gccagccct caggcacctc ggctgctcct cctgctgctg ctgcccgagg 686  
 ctctcctgct gatgtccact gcctgggtgcc tgcattggcg aaggaggcgg cggcggagggt 746  
 caccctaccc tggggagcag aggacactga ggcccagcga gcggagccat ctgcccgagg 806  
 acacagagct gggacctgga gggagtcagc tagagactgg tcccttcctc gaccacgcag 866  
 ccccgctcgc tccctcccca ggatcaaggc aacgccccgc cccaacgccc ccaaagccag 926  
 cccagcccc acctctcccc ctctgtacaa agtccttgcc cccaagaaat tgtatataaa 986  
 tcaccccttt ctaccaaaaa aaaaaaaaaa aaa 1019

<210> 34  
 <211> 31  
 <212> PRT  
 <213> Canis familiaris

<400> 34  
 Met Ile Val Leu Ala Pro Ala Trp Ser Pro Thr Val Arg Ile Pro Gly  
       1                          5                          10                          15  
 Gly Gln Gly Gly Gly Gln Ala Glu Arg Tyr Arg Ala Gly Gln Ser

<210> 35  
 <211> 1019  
 <212> DNA  
 <213> Canis familiaris

<400> 35  
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 actttgtaca gagggggaga ggtggggctg gggctggctt tgggggcgtt gggggcgggc 120  
 gttgccttga tcctggggag ggagcgagcg gggctgctg gtcgaggaag ggaccagtct 180  
 ctagctgact ccctccaggt ccagctctg tgcctcggg cagatggctc cgctcgctgg 240  
 gcctcagtgt cctctgctcc ccagggtagg gtgacctcg ccgccgctc cttcgccaat 300  
 gcaggcacca ggcagtggac atcagcagga gagccacggg cagcagcagc aggaggagca 360  
 gccgaggtgc ctgaggggct ggcaaggcag tggcctccag ggccccgggg ctcttgggg 420  
 gcaccaatgt agaggagtcg ggctgacact gcagctccag gcacccggag aaattcctgc 480  
 gggatgatcca gggcttcagg gcggccagct gctgggaggt gtcctggaag gcacagaagg 540  
 tgacaaagtg tatctccgtg ttgacagcct ccagcaggat ttgcatttgg gatccagcca 600  
 cagcctggag ccgcaccatc cagcgctggg ccaggaccag gcgccagaac gccccgcaga 660  
 gctcgtcgtc ctgcagggtg gaggcgacag tgactggata gtcctgaagc aggtaatcag 720  
 acagcttgcg gatggtgacc gcgaagggtg aggagatggg gctgtggctg aaggagcagt 780  
 cgggggtccc gcggaggccg gggctgagca gcagcagcag caacaggag gcctctgtcc 840  
 gtctgctctc tcagctctgc ccagctcggg agcgtctctg ctgtcccccg ccttgtcccc 900  
 cgggtatacg cacagttggg ctccaggctg gcgccagcac tatcatctcg gccggaggcc 960  
 cctcatgcct atggtcagat caggcttgcc ccagctgggc gtggaagggg ccaggccgg 1019

<210> 36  
 <211> 93  
 <212> DNA  
 <213> Canis familiaris

<400> 36  
 atgatagtgc tggcgccagc ctggagccca actgtgcgta taccggggg acaaggcggg 60  
 ggacaggcag agcgctaccg agctgggcag agc 93

<210> 37  
 <211> 93  
 <212> DNA  
 <213> Canis familiaris

<400> 37  
 gctctgccca gctcggtagc gctctgcctg tccccgcct tgtcccccg gtatacgcac 60  
 agttgggctc caggctggcg ccagcactat cat 93

<210> 38  
 <211> 27  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic  
 Primer

<400> 38  
 tgaattcgga cataacttca atattac 27

<210> 39  
 <211> 27  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic  
 Primer

<400> 39  
 tctcgagatt cagcttcaat gcctgta 27

<210> 40  
 <211> 28  
 <212> DNA  
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 40

cccaagctta tgggtctcac ctcccaac 28

<210> 41

<211> 395

<212> DNA

<213> Felis catus

<400> 41

ggccataggc atgaagggcc tccggccgag atgatagtgc tggcgccagc ctggagccca 60  
actacctccc tgctgctgct gctactgctc agccctggcc tccgcgggtc ccccgactgt 120  
tccttcagcc acagccccat ctctccacc ttcaagggtca ccatccgaaa gctgtctgat 180  
tacctgcttc aggattacc agtcaccgtc gcctccaacc tacaggacga cgagctctgt 240  
gggccattct ggcacctggt cctggcccag cgctggatgg gtcgggtcaa ggctgtggct 300  
gggtcccaga tgcaaagcct gctggaggcg gtcaacaccg agatacattt tgtcaccttg 360  
tgtgccttcc agcccctccc cagctgtctt cgatt 395

<210> 42

<211> 793

<212> DNA

<213> Felis catus

<400> 42

cttcaaggct accatccgaa agctgtctga ttacctgctt caggattacc cagtcaccgt 60  
cgctccaac ctacaggacg acgagctctg tgggccattc tggcacctgg tcctggccca 120  
gcgctggatg ggtcggtctca aggctgtggc tgggtcccag atgcaaagcc tgctggaggc 180  
ggtcaacacc gagatacatt ttgtcacctt gtgtgccttc cagcccctcc ccagctgtct 240  
tcgattcgtc cagaccaaca tctcccacct cctgcaggac acctccgagc agctggcggc 300  
cttgaagccc tggatcacc gcaggaattt ctcggggtgc ctggagctac agtgtcagcc 360

cgactcctcc accccactgc ccccaaggag ccccagggcc ttggaggcca cagccctgcc 420  
agccctcag gcccctctgc tgctcctcct gctgctgttg cctgtggctc tcttgctgat 480  
gtccgccgcc tggcgctgc actggcgaag aaggagatgg agaacgccct accccaggga 540  
gcagaggaag aactgaggc ccagagagag gaatcacctg cccgaggaca cagagccggg 600  
actcggagaa agtcagctag agactgggtc cttcctcgac cacgctgccc cgctcactct 660  
ccccccggga tggaggcaac gccagcccc aacgccagcc ccagaccac ctatccccct 720  
ctgtacaaag tccttgtcct caggaaattg tatataaatc atccttttct accaaaaaaa 780  
aaaaaaaaaa aaa 793

<210> 43  
<211> 942  
<212> DNA  
<213> Felis catus

<220>  
<221> CDS  
<222> (31)..(903)

<400> 43  
ggccataggc atgaagggcc tccggccgag atg ata gtg ctg gcg cca gcc tgg 54  
Met Ile Val Leu Ala Pro Ala Trp  
1 5  
agc cca act acc tcc ctg ctg ctg ctg cta ctg ctc agc cct ggc ctc 102  
Ser Pro Thr Thr Ser Leu Leu Leu Leu Leu Leu Leu Ser Pro Gly Leu  
10 15 20  
cgc ggg tcc ccc gac tgt tcc ttc agc cac agc ccc atc tcc tcc acc 150  
Arg Gly Ser Pro Asp Cys Ser Phe Ser His Ser Pro Ile Ser Ser Thr  
25 30 35 40  
ttc aag gtc acc atc cga aag ctg tct gat tac ctg ctt cag gat tac 198  
Phe Lys Val Thr Ile Arg Lys Leu Ser Asp Tyr Leu Leu Gln Asp Tyr  
45 50 55  
cca gtc acc gtc gcc tcc aac cta cag gac gac gag ctc tgt ggg cca 246  
Pro Val Thr Val Ala Ser Asn Leu Gln Asp Asp Glu Leu Cys Gly Pro  
60 65 70  
ttc tgg cac ctg gtc ctg gcc cag cgc tgg atg ggt cgg ctc aag gct 294

Phe	Trp	His	Leu	Val	Leu	Ala	Gln	Arg	Trp	Met	Gly	Arg	Leu	Lys	Ala	
		75					80					85				
gtg	gct	ggg	tcc	cag	atg	caa	agc	ctg	ctg	gag	gcg	gtc	aac	acc	gag	342
Val	Ala	Gly	Ser	Gln	Met	Gln	Ser	Leu	Leu	Glu	Ala	Val	Asn	Thr	Glu	
	90					95				100						
ata	cat	ttt	gtc	acc	ttg	tgt	gcc	ttc	cag	ccc	ctc	ccc	agc	tgt	ctt	390
Ile	His	Phe	Val	Thr	Leu	Cys	Ala	Phe	Gln	Pro	Leu	Pro	Ser	Cys	Leu	
105					110				115						120	
cga	ttc	gtc	cag	acc	aac	atc	tcc	cac	ctc	ctg	cag	gac	acc	tcc	gag	438
Arg	Phe	Val	Gln	Thr	Asn	Ile	Ser	His	Leu	Leu	Gln	Asp	Thr	Ser	Glu	
				125					130					135		
cag	ctg	gcg	gcc	ttg	aag	ccc	tgg	atc	acc	cgc	agg	aat	ttc	tcg	ggg	486
Gln	Leu	Ala	Ala	Leu	Lys	Pro	Trp	Ile	Thr	Arg	Arg	Asn	Phe	Ser	Gly	
			140					145					150			
tgc	ctg	gag	cta	cag	tgt	cag	ccc	gac	tcc	tcc	acc	cca	ctg	ccc	cca	534
Cys	Leu	Glu	Leu	Gln	Cys	Gln	Pro	Asp	Ser	Ser	Thr	Pro	Leu	Pro	Pro	
		155					160					165				
agg	agc	ccc	agg	gcc	ttg	gag	gcc	aca	gcc	ctg	cca	gcc	cct	cag	gcc	582
Arg	Ser	Pro	Arg	Ala	Leu	Glu	Ala	Thr	Ala	Leu	Pro	Ala	Pro	Gln	Ala	
	170					175					180					
cct	ctg	ctg	ctc	ctc	ctg	ctg	ctg	ttg	cct	gtg	gct	ctc	ttg	ctg	atg	630
Pro	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Leu	Pro	Val	Ala	Leu	Leu	Leu	Met	
185					190					195					200	
tcc	gcc	gcc	tgg	tgc	ctg	cac	tgg	cga	aga	agg	aga	tgg	aga	acg	ccc	678
Ser	Ala	Ala	Trp	Cys	Leu	His	Trp	Arg	Arg	Arg	Arg	Trp	Arg	Thr	Pro	
				205				210						215		
tac	ccc	agg	gag	cag	agg	aag	aca	ctg	agg	ccc	aga	gag	agg	aat	cac	726
Tyr	Pro	Arg	Glu	Gln	Arg	Lys	Thr	Leu	Arg	Pro	Arg	Glu	Arg	Asn	His	
			220					225					230			
ctg	ccc	gag	gac	aca	gag	ccg	gga	ctc	gga	gaa	agt	cag	cta	gag	act	774
Leu	Pro	Glu	Asp	Thr	Glu	Pro	Gly	Leu	Gly	Glu	Ser	Gln	Leu	Glu	Thr	
		235					240					245				
ggt	tcc	ttc	ctc	gac	cac	gct	gcc	ccg	ctc	act	ctc	ccc	ccg	gga	tgg	822
Gly	Ser	Phe	Leu	Asp	His	Ala	Ala	Pro	Leu	Thr	Leu	Pro	Pro	Gly	Trp	
	250					255					260					
agg	caa	cgc	cag	ccc	cca	acg	cca	gcc	cca	gac	cca	cct	atc	ccc	ctc	870

Arg Gln Arg Gln Pro Pro Thr Pro Ala Pro Asp Pro Pro Ile Pro Leu  
265 270 275 280

tgt aca aag tcc ttg tcc tca gga aat tgt ata taaatcatcc ttttctacca 923  
Cys Thr Lys Ser Leu Ser Ser Gly Asn Cys Ile  
285 290

aaaaaaaaaa aaaaaaaaaa 942

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<212> PRT  
<213> Felis catus

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35 40 45

Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val Thr Val Ala Ser Asn Leu  
50 55 60

Gln Asp Asp Glu Leu Cys Gly Pro Phe Trp His Leu Val Leu Ala Gln  
65 70 75 80

Arg Trp Met Gly Arg Leu Lys Ala Val Ala Gly Ser Gln Met Gln Ser  
85 90 95

Leu Leu Glu Ala Val Asn Thr Glu Ile His Phe Val Thr Leu Cys Ala  
100 105 110

Phe Gln Pro Leu Pro Ser Cys Leu Arg Phe Val Gln Thr Asn Ile Ser  
115 120 125

His Leu Leu Gln Asp Thr Ser Glu Gln Leu Ala Ala Leu Lys Pro Trp  
130 135 140

Ile Thr Arg Arg Asn Phe Ser Gly Cys Leu Glu Leu Gln Cys Gln Pro  
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Asp Ser Ser Thr Pro Leu Pro Pro Arg Ser Pro Arg Ala Leu Glu Ala  
165 170 175



Thr Ala Leu Pro Ala Pro Gln Ala Pro Leu Leu Leu Leu Leu Leu Leu  
 180 185 190

Leu Pro Val Ala Leu Leu Leu Met Ser Ala Ala Trp Cys Leu His Trp  
 195 200 205

Arg Arg Arg Arg Trp Arg Thr Pro Tyr Pro Arg Glu Gln Arg Lys Thr  
 210 215 220

Leu Arg Pro Arg Glu Arg Asn His Leu Pro Glu Asp Thr Glu Pro Gly  
 225 230 235 240

Leu Gly Glu Ser Gln Leu Glu Thr Gly Ser Phe Leu Asp His Ala Ala  
 245 250 255

Pro Leu Thr Leu Pro Pro Gly Trp Arg Gln Arg Gln Pro Pro Thr Pro  
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Ala Pro Asp Pro Pro Ile Pro Leu Cys Thr Lys Ser Leu Ser Ser Gly  
 275 280 285

Asn Cys Ile  
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 <213> Felis catus

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gaggccaggg ctgagcagta gcagcagcag cagggaggta gttgggctcc aggctggcgc 900  
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<220>

<221> CDS

<222> (1)..(795)

<400> 48

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1				5					10					15		

gtc	acc	atc	cga	aag	ctg	tct	gat	tac	ctg	ctt	cag	gat	tac	cca	gtc	96
Val	Thr	Ile	Arg	Lys	Leu	Ser	Asp	Tyr	Leu	Leu	Gln	Asp	Tyr	Pro	Val	
			20					25					30			

acc	gtc	gcc	tcc	aac	cta	cag	gac	gac	gag	ctc	tgt	ggg	cca	ttc	tgg	144
Thr	Val	Ala	Ser	Asn	Leu	Gln	Asp	Asp	Glu	Leu	Cys	Gly	Pro	Phe	Trp	
		35					40					45				

cac	ctg	gtc	ctg	gcc	cag	cgc	tgg	atg	ggg	cgg	ctc	aag	gct	gtg	gct	192
His	Leu	Val	Leu	Ala	Gln	Arg	Trp	Met	Gly	Arg	Leu	Lys	Ala	Val	Ala	
	50					55					60					

ggg	tcc	cag	atg	caa	agc	ctg	ctg	gag	gcg	gtc	aac	acc	gag	ata	cat	240
Gly	Ser	Gln	Met	Gln	Ser	Leu	Leu	Glu	Ala	Val	Asn	Thr	Glu	Ile	His	
65					70				75					80		

ttt	gtc	acc	ttg	tgt	gcc	ttc	cag	ccc	ctc	ccc	agc	tgt	ctt	cga	ttc	288
Phe	Val	Thr	Leu	Cys	Ala	Phe	Gln	Pro	Leu	Pro	Ser	Cys	Leu	Arg	Phe	
				85				90						95		

gtc	cag	acc	aac	atc	tcc	cac	ctc	ctg	cag	gac	acc	tcc	gag	cag	ctg	336
Val	Gln	Thr	Asn	Ile	Ser	His	Leu	Leu	Gln	Asp	Thr	Ser	Glu	Gln	Leu	
			100					105					110			

gcg	gcc	ttg	aag	ccc	tgg	atc	acc	cgc	agg	aat	ttc	tcg	ggg	tgc	ctg	384
Ala	Ala	Leu	Lys	Pro	Trp	Ile	Thr	Arg	Arg	Asn	Phe	Ser	Gly	Cys	Leu	
		115					120					125				

gag	cta	cag	tgt	cag	ccc	gac	tcc	tcc	acc	cca	ctg	ccc	cca	agg	agc	432
Glu	Leu	Gln	Cys	Gln	Pro	Asp	Ser	Ser	Thr	Pro	Leu	Pro	Pro	Arg	Ser	
	130					135					140					

ccc	agg	gcc	ttg	gag	gcc	aca	gcc	ctg	cca	gcc	cct	cag	gcc	cct	ctg	480
Pro	Arg	Ala	Leu	Glu	Ala	Thr	Ala	Leu	Pro	Ala	Pro	Gln	Ala	Pro	Leu	
145					150					155					160	

ctg	ctc	ctc	ctg	ctg	ctg	ttg	cct	gtg	gct	ctc	ttg	ctg	atg	tcc	gcc	528
Leu	Leu	Leu	Leu	Leu	Leu	Leu	Pro	Val	Ala	Leu	Leu	Leu	Met	Ser	Ala	
				165					170					175		

gcc tgg tgc ctg cac tgg cga aga agg aga tgg aga acg ccc tac ccc 576  
 Ala Trp Cys Leu His Trp Arg Arg Arg Arg Trp Arg Thr Pro Tyr Pro  
                   180                          185                          190

agg gag cag agg aag aca ctg agg ccc aga gag agg aat cac ctg ccc 624  
 Arg Glu Gln Arg Lys Thr Leu Arg Pro Arg Glu Arg Asn His Leu Pro  
                   195                          200                          205

gag gac aca gag ccg gga ctc gga gaa agt cag cta gag act ggt tcc 672  
 Glu Asp Thr Glu Pro Gly Leu Gly Glu Ser Gln Leu Glu Thr Gly Ser  
                   210                          215                          220

ttc ctc gac cac gct gcc ccg ctc act ctc ccc ccg gga tgg agg caa 720  
 Phe Leu Asp His Ala Ala Pro Leu Thr Leu Pro Pro Gly Trp Arg Gln  
 225                          230                          235                          240

cgc cag ccc cca acg cca gcc cca gac cca cct atc ccc ctc tgt aca 768  
 Arg Gln Pro Pro Thr Pro Ala Pro Asp Pro Pro Ile Pro Leu Cys Thr  
                           245                          250                          255

aag tcc ttg tcc tca gga aat tgt ata 795  
 Lys Ser Leu Ser Ser Gly Asn Cys Ile  
                   260                          265

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 <212> PRT  
 <213> Felis catus

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Val Thr Ile Arg Lys Leu Ser Asp Tyr Leu Leu Gln Asp Tyr Pro Val  
                   20                          25                          30

Thr Val Ala Ser Asn Leu Gln Asp Asp Glu Leu Cys Gly Pro Phe Trp  
                   35                          40                          45

His Leu Val Leu Ala Gln Arg Trp Met Gly Arg Leu Lys Ala Val Ala  
                   50                          55                          60

Gly Ser Gln Met Gln Ser Leu Leu Glu Ala Val Asn Thr Glu Ile His  
   65                          70                          75                          80

Phe Val Thr Leu Cys Ala Phe Gln Pro Leu Pro Ser Cys Leu Arg Phe

	85	90	95
Val Gln Thr Asn Ile Ser His Leu Leu Gln Asp Thr Ser Glu Gln Leu	100	105	110
Ala Ala Leu Lys Pro Trp Ile Thr Arg Arg Asn Phe Ser Gly Cys Leu	115	120	125
Glu Leu Gln Cys Gln Pro Asp Ser Ser Thr Pro Leu Pro Pro Arg Ser	130	135	140
Pro Arg Ala Leu Glu Ala Thr Ala Leu Pro Ala Pro Gln Ala Pro Leu	145	150	155
Leu Leu Leu Leu Leu Leu Leu Pro Val Ala Leu Leu Leu Met Ser Ala	165	170	175
Ala Trp Cys Leu His Trp Arg Arg Arg Arg Trp Arg Thr Pro Tyr Pro	180	185	190
Arg Glu Gln Arg Lys Thr Leu Arg Pro Arg Glu Arg Asn His Leu Pro	195	200	205
Glu Asp Thr Glu Pro Gly Leu Gly Glu Ser Gln Leu Glu Thr Gly Ser	210	215	220
Phe Leu Asp His Ala Ala Pro Leu Thr Leu Pro Pro Gly Trp Arg Gln	225	230	235
Arg Gln Pro Pro Thr Pro Ala Pro Asp Pro Pro Ile Pro Leu Cys Thr	245	250	255
Lys Ser Leu Ser Ser Gly Asn Cys Ile	260	265	

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 gaaggaacca gtctctagct gactttctcc gagtcccggc tctgtgtcct cgggcaggtg 180

attcctctct ctgggcctca gtgtcttcct ctgctccctg gggtagggcg ttctccatct 240  
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 cccacagagc tcgtcgtcct gtaggttgga ggcgacggtg actgggtaat cctgaagcag 720  
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 <212> DNA  
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<220>



<221> CDS  
 <222> (196)..(1017)

<400> 52

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gctattcacc tcgcc atg gtt ctc ctg cct ctg cgc tgt ctc ttc tgg ggc 231
      Met Val Leu Leu Pro Leu Arg Cys Leu Phe Trp Gly
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tcc ttg ttg acc acc gtc tac cca gaa cca cgc act gca tgc aga gaa 279
Ser Leu Leu Thr Thr Val Tyr Pro Glu Pro Arg Thr Ala Cys Arg Glu
              15              20              25

aag caa tac cta gta gac agt cag tgc tgt aat atg tgc cca cca gga 327
Lys Gln Tyr Leu Val Asp Ser Gln Cys Cys Asn Met Cys Pro Pro Gly
              30              35              40

gag aaa ctg gtg aat gac tgc cta cat acc att gac acg gaa tgc act 375
Glu Lys Leu Val Asn Asp Cys Leu His Thr Ile Asp Thr Glu Cys Thr
              45              50              55              60

cgt tgc caa aca ggc gaa ttc cta gac act tgg aac gca gag aga cac 423
Arg Cys Gln Thr Gly Glu Phe Leu Asp Thr Trp Asn Ala Glu Arg His
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tgt cac cag cac aaa tac tgc gac ccc aac cta ggg ctc cat gtc gag 471
Cys His Gln His Lys Tyr Cys Asp Pro Asn Leu Gly Leu His Val Glu
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aag gag ggc acg tca gaa aca gac acc act tgc aca tgc gat gaa ggt 519
Lys Glu Gly Thr Ser Glu Thr Asp Thr Thr Cys Thr Cys Asp Glu Gly
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ctg cat tgt acc aac gct gcc tgt gag agc tgc acc atg cac agc ctg 567
Leu His Cys Thr Asn Ala Ala Cys Glu Ser Cys Thr Met His Ser Leu
              110              115              120

tgc ccc cct ggc ctg gga gtc aaa cag atc gct aca ggg att tct gat 615
Cys Pro Pro Gly Leu Gly Val Lys Gln Ile Ala Thr Gly Ile Ser Asp
              125              130              135              140

acc atc tgc gat ccc tgc ccc atc ggc ttc ttc tcc aat gtg tct tct 663
Thr Ile Cys Asp Pro Cys Pro Ile Gly Phe Phe Ser Asn Val Ser Ser
  
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Ala Leu Glu Lys Cys His Pro Trp Thr Ser Cys Glu Thr Lys Gly Leu			
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gtg aag gtt cag gcg gga act aac aag act gat gtt atc tgt ggt ccc			759
Val Lys Val Gln Ala Gly Thr Asn Lys Thr Asp Val Ile Cys Gly Pro			
175	180	185	
cag cct cgg tta aga gcc cta gtg gtg gtc ccc atc att atg ggg atc			807
Gln Pro Arg Leu Arg Ala Leu Val Val Val Pro Ile Ile Met Gly Ile			
190	195	200	
ctg ctt gtt gtc ctg ttg gtg tct gcc tgc atc cga aag gtg gtc aag			855
Leu Leu Val Val Leu Leu Val Ser Ala Cys Ile Arg Lys Val Val Lys			
205	210	215	220
aag cca gag aat aag gtt atg tat cag gac cct gtg gag gac ttg gag			903
Lys Pro Glu Asn Lys Val Met Tyr Gln Asp Pro Val Glu Asp Leu Glu			
225	230	235	
gaa ttt cct atg ccc ccg cac tcc att gct ccg gtg caa gag acc tta			951
Glu Phe Pro Met Pro Pro His Ser Ile Ala Pro Val Gln Glu Thr Leu			
240	245	250	
cat ggg tgc cag ccc gtc acc cag gag gac ggc aaa gag agc cgc atc			999
His Gly Cys Gln Pro Val Thr Gln Glu Asp Gly Lys Glu Ser Arg Ile			
255	260	265	
tcc gtg cag gag aga gtg tgaggcagcg tgtgccagg agtgtgacag			1047
Ser Val Gln Glu Arg Val			
270			
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 <212> PRT  
 <213> Canis familiaris

<400> 53

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			20					25					30		
Val	Asp	Ser	Gln	Cys	Cys	Asn	Met	Cys	Pro	Pro	Gly	Glu	Lys	Leu	Val
		35					40					45			
Asn	Asp	Cys	Leu	His	Thr	Ile	Asp	Thr	Glu	Cys	Thr	Arg	Cys	Gln	Thr
	50					55					60				
Gly	Glu	Phe	Leu	Asp	Thr	Trp	Asn	Ala	Glu	Arg	His	Cys	His	Gln	His
65					70					75					80
Lys	Tyr	Cys	Asp	Pro	Asn	Leu	Gly	Leu	His	Val	Glu	Lys	Glu	Gly	Thr
				85					90					95	
Ser	Glu	Thr	Asp	Thr	Thr	Cys	Thr	Cys	Asp	Glu	Gly	Leu	His	Cys	Thr
			100					105					110		
Asn	Ala	Ala	Cys	Glu	Ser	Cys	Thr	Met	His	Ser	Leu	Cys	Pro	Pro	Gly
		115					120					125			
Leu	Gly	Val	Lys	Gln	Ile	Ala	Thr	Gly	Ile	Ser	Asp	Thr	Ile	Cys	Asp
	130					135					140				
Pro	Cys	Pro	Ile	Gly	Phe	Phe	Ser	Asn	Val	Ser	Ser	Ala	Leu	Glu	Lys
145				150						155				160	
Cys	His	Pro	Trp	Thr	Ser	Cys	Glu	Thr	Lys	Gly	Leu	Val	Lys	Val	Gln
				165					170					175	
Ala	Gly	Thr	Asn	Lys	Thr	Asp	Val	Ile	Cys	Gly	Pro	Gln	Pro	Arg	Leu
			180					185					190		
Arg	Ala	Leu	Val	Val	Val	Pro	Ile	Ile	Met	Gly	Ile	Leu	Leu	Val	Val
		195				200						205			
Leu	Leu	Val	Ser	Ala	Cys	Ile	Arg	Lys	Val	Val	Lys	Lys	Pro	Glu	Asn
	210					215					220				

Lys Val Met Tyr Gln Asp Pro Val Glu Asp Leu Glu Glu Phe Pro Met  
 225 230 235 240

Pro Pro His Ser Ile Ala Pro Val Gln Glu Thr Leu His Gly Cys Gln  
 245 250 255

Pro Val Thr Gln Glu Asp Gly Lys Glu Ser Arg Ile Ser Val Gln Glu  
 260 265 270

Arg Val

<210> 54

<211> 1425

<212> DNA

<213> Canis familiaris

<400> 54

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 tgaacagcta agtggcctcc agttgtccac tgtcacaaac aatgccacaa tggctcttcg 120  
 tgggtcttcc tgggctcgta gaaaccaccg tgatatacac ctgagggcc tgaaatgctg 180  
 ggttggtgga tattactatc tggcccccca aaagtttcat ctccatcttt aaaagcaagt 240  
 tgggaggtgg aatgggctcc aggggtgggg tggaagggtc tctgtttctg cagcacaggg 300  
 gtgcaggcag gggagcaccg ccccttcatg cccctccagc agtccaggc tctccagcca 360  
 cgcgcccact ctcccacgct gtcacactcc tgggcacacg ctgcctcaca ctctctcctg 420  
 cacggagatg cggctctctt tgccgtcctc ctgggtgacg ggctggcacc catgtaaggt 480  
 ctcttgcacc ggagcaatgg agtgcggggg cataggaaat tcctccaagt cctccacagg 540  
 gtcttgatac ataaccttat tctctggctt cttgaccacc tttcggatgc aggcagacac 600  
 caacaggaca acaagcagga tccccataat gatggggacc accactaggg ctcttaaccg 660  
 aggctgggga ccacagataa catcagtctt gttagttccc gcctgaacct tcaccaggcc 720  
 tttggtttca cagcttgtcc aagggtgaca cttttccaaa gcagaagaca cattggagaa 780  
 gaagccgatg gggcagggat cgcagatggt atcagaaatc cctgtagcga tctgtttgac 840

tcccaggcca ggggggcaca ggctgtgcat ggtgcagctc tcacaggcag cgttggtaca 900  
atgcagacct tcattcgcatg tgcaagtggg gtctgtttct gacgtgccct ccttctcgac 960  
atggagccct aggttggggg cgcagtatct gtgctgggtga cagtgtctct ctgcgttcca 1020  
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gtcattcacc agtttctctc ctgggtgggca catattacag cactgactgt ctactaggta 1140  
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gaagagacag cgcagaggca ggagaacccat ggcgaggtga atagcaggca gcggagtagg 1260  
ggcgcgggga tgtctttagt aactccccag cccttgcccc cgcgcgcgcg gccagaggaga 1320  
tgggcggggg ctteggggac caatcgtggc cggcttcgtt gggcagggcg gagctcctgg 1380  
agacccttag cgcggggagt tcccctgaat attcccgga gtcta 1425

<210> 55  
<211> 822  
<212> DNA  
<213> Canis familiaris

<400> 55  
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gaaccacgca ctgcatgcag agaaaagcaa tacctagtag acagtcagtg ctgtaatatg 120  
tgcccaccag gagagaaact ggtgaatgac tgcctacata ccattgacac ggaatgcact 180  
cgttgccaaa caggcgaatt cctagacact tggaacgcag agagacactg tcaccagcac 240  
aaatactgcg accccaacct agggctccat gtcgagaagg agggcacgtc agaaacagac 300  
accacttgca catgcgatga aggtctgcat tgtaccaacg ctgcctgtga gagctgcacc 360  
atgcacagcc tgtgcccccc tggcctggga gtcaaacaga tcgctacagg gatttctgat 420  
accatctgcg atccctgccc catcggcttc ttctccaatg tgtcttctgc tttggaaaag 480  
tgtcaccctt ggacaagctg tgaaaccaa ggctgtgtga aggttcaggc gggaactaac 540  
aagactgatg ttatctgtgg tcccagcct cggttaagag ccctagtggg ggtccccatc 600  
attatgggga tcctgcttgt tgcctgttg gtgtctgcct gcatccgaaa ggtgggtcaag 660

aagccagaga ataaggttat gtatcaggac cctgtggagg acttggagga atttcctatg 720  
 cccccgcact ccattgctcc ggtgcaagag accttacatg ggtgccagcc cgtcaccag 780  
 gaggacggca aagagagccg catctccgtg caggagagag tg 822

<210> 56  
 <211> 822  
 <212> DNA  
 <213> Canis familiaris

<400> 56  
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 cccatgtaag gtctcttgca ccggagcaat ggagtgcggg ggcataggaa attcctccaa 120  
 gtcctccaca gggtcctgat acataacctt attctctggc ttcttgacca cctttcggat 180  
 gcaggcagac accaacagga caacaagcag gatccccata atgatgggga ccaccactag 240  
 ggctcttaac cgaggctggg gaccacagat aacatcagtc ttgttagttc ccgcctgaac 300  
 cttcaccagg ccttttggtt cacagcttgt ccaaggggtga cacttttcca aagcagaaga 360  
 cacattggag aagaagccga tggggcaggg atcgcagatg gtatcagaaa tccctgtagc 420  
 gatctgtttg actcccaggc caggggggca caggctgtgc atgggtgcagc tctcacaggc 480  
 agcgttggtg caatgcagac cttcatcgca tgtgcaagtg gtgtctgttt ctgacgtgcc 540  
 ctcttctcg acatggagcc ctaggttggg gtcgcagtat ttgtgctggg gacagtgtct 600  
 ctctgcgttc caagtgtcta ggaattcgcc tgtttggcaa cgagtgcatt ccgtgtcaat 660  
 ggtatgtagg cagtcattca ccagtttctc tcctgggtggg cacatattac agcactgact 720  
 gtctactagg tattgctttt ctctgcatgc agtgcggtgt tctgggtaga cgggtgggtcaa 780  
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<210> 57  
 <211> 765  
 <212> DNA  
 <213> Canis familiaris

<220>

<221> CDS

<222> (1)..(765)

<400> 57

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cag tgc tgt aat atg tgc cca cca gga gag aaa ctg gtg aat gac tgc	96
Gln Cys Cys Asn Met Cys Pro Pro Gly Glu Lys Leu Val Asn Asp Cys	
20 25 30	
cta cat acc att gac acg gaa tgc act cgt tgc caa aca ggc gaa ttc	144
Leu His Thr Ile Asp Thr Glu Cys Thr Arg Cys Gln Thr Gly Glu Phe	
35 40 45	
cta gac act tgg aac gca gag aga cac tgt cac cag cac aaa tac tgc	192
Leu Asp Thr Trp Asn Ala Glu Arg His Cys His Gln His Lys Tyr Cys	
50 55 60	
gac ccc aac cta ggg ctc cat gtc gag aag gag ggc acg tca gaa aca	240
Asp Pro Asn Leu Gly Leu His Val Glu Lys Glu Gly Thr Ser Glu Thr	
65 70 75 80	
gac acc act tgc aca tgc gat gaa ggt ctg cat tgt acc aac gct gcc	288
Asp Thr Thr Cys Thr Cys Asp Glu Gly Leu His Cys Thr Asn Ala Ala	
85 90 95	
tgt gag agc tgc acc atg cac agc ctg tgc ccc cct ggc ctg gga gtc	336
Cys Glu Ser Cys Thr Met His Ser Leu Cys Pro Pro Gly Leu Gly Val	
100 105 110	
aaa cag atc gct aca ggg att tct gat acc atc tgc gat ccc tgc ccc	384
Lys Gln Ile Ala Thr Gly Ile Ser Asp Thr Ile Cys Asp Pro Cys Pro	
115 120 125	
atc ggc ttc ttc tcc aat gtg tct tct gct ttg gaa aag tgt cac cct	432
Ile Gly Phe Phe Ser Asn Val Ser Ser Ala Leu Glu Lys Cys His Pro	
130 135 140	
tgg aca agc tgt gaa acc aaa ggc ctg gtg aag gtt cag gcg gga act	480
Trp Thr Ser Cys Glu Thr Lys Gly Leu Val Lys Val Gln Ala Gly Thr	
145 150 155 160	
aac aag act gat gtt atc tgt ggt ccc cag cct cgg tta aga gcc cta	528
Asn Lys Thr Asp Val Ile Cys Gly Pro Gln Pro Arg Leu Arg Ala Leu	
165 170 175	



gtg gtg gtc ccc atc att atg ggg atc ctg ctt gtt gtc ctg ttg gtg 576  
 Val Val Val Pro Ile Ile Met Gly Ile Leu Leu Val Val Leu Leu Val  
 180 185 190

tct gcc tgc atc cga aag gtg gtc aag aag cca gag aat aag gtt atg 624  
 Ser Ala Cys Ile Arg Lys Val Val Lys Lys Pro Glu Asn Lys Val Met  
 195 200 205

tat cag gac cct gtg gag gac ttg gag gaa ttt cct atg ccc ccg cac 672  
 Tyr Gln Asp Pro Val Glu Asp Leu Glu Glu Phe Pro Met Pro Pro His  
 210 215 220

tcc att gct ccg gtg caa gag acc tta cat ggg tgc cag ccc gtc acc 720  
 Ser Ile Ala Pro Val Gln Glu Thr Leu His Gly Cys Gln Pro Val Thr  
 225 230 235 240

cag gag gac ggc aaa gag agc cgc atc tcc gtg cag gag aga gtg 765  
 Gln Glu Asp Gly Lys Glu Ser Arg Ile Ser Val Gln Glu Arg Val  
 245 250 255

<210> 58  
 <211> 255  
 <212> PRT  
 <213> Canis familiaris

<400> 58  
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Gln Cys Cys Asn Met Cys Pro Pro Gly Glu Lys Leu Val Asn Asp Cys  
 20 25 30

Leu His Thr Ile Asp Thr Glu Cys Thr Arg Cys Gln Thr Gly Glu Phe  
 35 40 45

Leu Asp Thr Trp Asn Ala Glu Arg His Cys His Gln His Lys Tyr Cys  
 50 55 60

Asp Pro Asn Leu Gly Leu His Val Glu Lys Glu Gly Thr Ser Glu Thr  
 65 70 75 80

Asp Thr Thr Cys Thr Cys Asp Glu Gly Leu His Cys Thr Asn Ala Ala  
 85 90 95

Cys Glu Ser Cys Thr Met His Ser Leu Cys Pro Pro Gly Leu Gly Val  
 100 105 110

Lys Gln Ile Ala Thr Gly Ile Ser Asp Thr Ile Cys Asp Pro Cys Pro  
 115 120 125  
 Ile Gly Phe Phe Ser Asn Val Ser Ser Ala Leu Glu Lys Cys His Pro  
 130 135 140  
 Trp Thr Ser Cys Glu Thr Lys Gly Leu Val Lys Val Gln Ala Gly Thr  
 145 150 155 160  
 Asn Lys Thr Asp Val Ile Cys Gly Pro Gln Pro Arg Leu Arg Ala Leu  
 165 170 175  
 Val Val Val Pro Ile Ile Met Gly Ile Leu Leu Val Val Leu Leu Val  
 180 185 190  
 Ser Ala Cys Ile Arg Lys Val Val Lys Lys Pro Glu Asn Lys Val Met  
 195 200 205  
 Tyr Gln Asp Pro Val Glu Asp Leu Glu Glu Phe Pro Met Pro Pro His  
 210 215 220  
 Ser Ile Ala Pro Val Gln Glu Thr Leu His Gly Cys Gln Pro Val Thr  
 225 230 235 240  
 Gln Glu Asp Gly Lys Glu Ser Arg Ile Ser Val Gln Glu Arg Val  
 245 250 255

<210> 59  
 <211> 765  
 <212> DNA  
 <213> Canis familiaris

<400> 59  
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 gtctccaca gggtcctgat acataacctt attctctggc ttcttgacca cctttcggat 180  
 gcaggcagac accaacagga caacaagcag gatccccata atgatgggga ccaccactag 240  
 ggctcttaac cgaggctggg gaccacagat aacatcagtc ttgttagttc ccgcctgaac 300  
 cttcaccagg cctttggttt cacagcttgt ccaagggtga cacttttcca aagcagaaga 360  
 cacattggag aagaagccga tggggcaggg atcgcagatg gtatcagaaa tccctgtagc 420

gatctgtttg actcccaggc cagggggggca caggctgtgc atggtgcagc tctcacaggc 480  
agcgttggtg caatgcagac cttcatcgca tgtgcaagtg gtgtctgttt ctgacgtgcc 540  
ctccttctcg acatggagcc ctaggttggg gtcgcagtat ttgtgctggt gacagtgtct 600  
ctctgcgttc caagtgtcta ggaattcgcc tgtttggtgaa cgagtgcatt ccgtgtcaat 660  
ggtatgtagg cagtcattca ccagtttctc tcctgggtggg cacatattac agcactgact 720  
gtctactagg tattgctttt ctctgcatgc agtgcgtggt tctgg 765

<210> 60  
<211> 336  
<212> DNA  
<213> Felis catus

<220>  
<221> CDS  
<222> (1)..(336)

<400> 60  
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Asn Val Ser Ser Ala Ser Glu Lys Cys His Pro Trp Thr Arg Cys Glu  
1 5 10 15  
  
acc aaa ggc ctg gtg gag ctt cag gcg ggg acc aac aag acg gat gcc 96  
Thr Lys Gly Leu Val Glu Leu Gln Ala Gly Thr Asn Lys Thr Asp Ala  
20 25 30  
  
gtc tgc ggt ttc cag gat cgg ata aga gcc ctg gtg gtg atc ccc atc 144  
Val Cys Gly Phe Gln Asp Arg Ile Arg Ala Leu Val Val Ile Pro Ile  
35 40 45  
  
acg atg gtg gtc ctg ctt gct gtc ttg ttg gtg tct gcg tat atc aga 192  
Thr Met Val Val Leu Leu Ala Val Leu Leu Val Ser Ala Tyr Ile Arg  
50 55 60  
  
aag gtg acc aag aag cca gag aat aag gtc ctc cag cct aag gct gtg 240  
Lys Val Thr Lys Lys Pro Glu Asn Lys Val Leu Gln Pro Lys Ala Val  
65 70 75 80  
  
tcg cag gac cct gtg gag gac ttg gag gtc ctt cct gtc ccc ctc cac 288  
Ser Gln Asp Pro Val Glu Asp Leu Glu Val Leu Pro Val Pro Leu His  
85 90 95

ccc att gct ccg gtg cag gag acc tta cac ggg tgc cag ccg gtc acc 336  
 Pro Ile Ala Pro Val Gln Glu Thr Leu His Gly Cys Gln Pro Val Thr  
 100 105 110

<210> 61  
 <211> 112  
 <212> PRT  
 <213> Felis catus

<400> 61  
 Asn Val Ser Ser Ala Ser Glu Lys Cys His Pro Trp Thr Arg Cys Glu  
 1 5 10 15  
 Thr Lys Gly Leu Val Glu Leu Gln Ala Gly Thr Asn Lys Thr Asp Ala  
 20 25 30  
 Val Cys Gly Phe Gln Asp Arg Ile Arg Ala Leu Val Val Ile Pro Ile  
 35 40 45  
 Thr Met Val Val Leu Leu Ala Val Leu Leu Val Ser Ala Tyr Ile Arg  
 50 55 60  
 Lys Val Thr Lys Lys Pro Glu Asn Lys Val Leu Gln Pro Lys Ala Val  
 65 70 75 80  
 Ser Gln Asp Pro Val Glu Asp Leu Glu Val Leu Pro Val Pro Leu His  
 85 90 95  
 Pro Ile Ala Pro Val Gln Glu Thr Leu His Gly Cys Gln Pro Val Thr  
 100 105 110

<210> 62  
 <211> 336  
 <212> DNA  
 <213> Felis catus

<400> 62  
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 attctctggc ttcttgggtca cctttctgat atacgcagac accaacaaga cagcaagcag 180  
 gaccaccatc gtgatgggga tcaccaccag ggctcttata cgatcctgga aaccgcagac 240  
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ccaaggggtga cacttttccg aagcagatga cacatt 336

<210> 63  
<211> 390  
<212> DNA  
<213> Canis familiaris

<400> 63  
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accataagca gcaacctggt gagcctcgag aatgggaaac agttggccgt gaaaagacaa 120  
ggactctatt acgtctatgc ccaagtcacc ttctgctcca atcgggcagc ttcgagtcaa 180  
gctccgttcg tcgccagcct atgcctccat tccccgagtg gaacggagag agtcttactc 240  
cgcgccgcga gctcccgcgg ctcgctccaaa ccttgccggcc aacagtccat ccacttggga 300  
ggagtatttg aattgcatcc aggtgcttcg gtgttcgtca acgtgactga tccaagccaa 360  
gtgagccacg ggaccggcct cacgtctttt 390

<210> 64  
<211> 1878  
<212> DNA  
<213> Canis familiaris

<220>  
<221> CDS  
<222> (284)..(1063)

<400> 64  
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tttgctggga gagaagacta cgaagcacat tttccaggaa gtgtgggctg caacgattgt 180  
gcgctcttaa ctaatcctga gtaagggtggc cactttgaca gtgttttcat gctgcctctg 240  
ccaccttctc ggtctgaaga tatcatttca actctaacac agc atg atc gaa aca 295  
Met Ile Glu Thr

1

tat agc caa act gct ccc cga tct gtg gcc act gga cca ccc gtc agt 343

Tyr	Ser	Gln	Thr	Ala	Pro	Arg	Ser	Val	Ala	Thr	Gly	Pro	Pro	Val	Ser	
5					10					15					20	
atg	aaa	att	ttt	atg	tat	ttg	ctt	act	ggt	ttt	ctc	atc	acc	cag	atg	391
Met	Lys	Ile	Phe	Met	Tyr	Leu	Leu	Thr	Val	Phe	Leu	Ile	Thr	Gln	Met	
				25					30					35		
att	gga	tcg	gca	ctc	ttt	gct	gta	tat	ctt	cac	aga	aga	ttg	gac	aag	439
Ile	Gly	Ser	Ala	Leu	Phe	Ala	Val	Tyr	Leu	His	Arg	Arg	Leu	Asp	Lys	
			40					45					50			
ata	gaa	gat	gaa	agg	aat	ctt	tat	gaa	gat	ttt	gtg	ttc	atg	aaa	acg	487
Ile	Glu	Asp	Glu	Arg	Asn	Leu	Tyr	Glu	Asp	Phe	Val	Phe	Met	Lys	Thr	
		55					60					65				
tta	cag	aaa	tgc	aac	aaa	ggg	gag	ggg	tcc	ttg	tcc	tta	ctg	aac	tgt	535
Leu	Gln	Lys	Cys	Asn	Lys	Gly	Glu	Gly	Ser	Leu	Ser	Leu	Leu	Asn	Cys	
	70					75					80					
gag	gaa	att	aaa	agc	caa	ttt	gaa	gcc	ttt	ctc	aag	gag	ata	atg	cta	583
Glu	Glu	Ile	Lys	Ser	Gln	Phe	Glu	Ala	Phe	Leu	Lys	Glu	Ile	Met	Leu	
	85				90				95					100		
aac	aac	gaa	atg	aag	aaa	gaa	gaa	aac	att	gca	atg	caa	aaa	ggt	gat	631
Asn	Asn	Glu	Met	Lys	Lys	Glu	Glu	Asn	Ile	Ala	Met	Gln	Lys	Gly	Asp	
				105				110					115			
cag	gat	cct	cga	att	gca	gcc	cat	gtc	ata	agt	gag	gct	agt	agt	aac	679
Gln	Asp	Pro	Arg	Ile	Ala	Ala	His	Val	Ile	Ser	Glu	Ala	Ser	Ser	Asn	
			120					125					130			
cca	gcg	tcc	gtt	ctg	cgg	tgg	gcg	cca	aaa	ggg	tac	tac	acc	ata	agc	727
Pro	Ala	Ser	Val	Leu	Arg	Trp	Ala	Pro	Lys	Gly	Tyr	Tyr	Thr	Ile	Ser	
		135				140						145				
agc	aac	ctg	gtg	agc	ctc	gag	aat	ggg	aaa	cag	ttg	gcc	gtg	aaa	aga	775
Ser	Asn	Leu	Val	Ser	Leu	Glu	Asn	Gly	Lys	Gln	Leu	Ala	Val	Lys	Arg	
	150					155				160						
caa	gga	ctc	tat	tac	gtc	tat	gcc	caa	gtc	acc	ttc	tgc	tcc	aat	cgg	823
Gln	Gly	Leu	Tyr	Tyr	Val	Tyr	Ala	Gln	Val	Thr	Phe	Cys	Ser	Asn	Arg	
	165				170				175					180		
gca	gct	tcg	agt	caa	gct	ccg	ttc	gtc	gcc	agc	cta	tgc	ctc	cat	tcc	871
Ala	Ala	Ser	Ser	Gln	Ala	Pro	Phe	Val	Ala	Ser	Leu	Cys	Leu	His	Ser	
				185				190						195		
ccg	agt	gga	acg	gag	aga	gtc	tta	ctc	cgc	gcc	gcg	agc	tcc	cgc	ggc	919

Pro Ser Gly Thr Glu Arg Val Leu Leu Arg Ala Ala Ser Ser Arg Gly  
 200 205 210

tcg tcc aaa cct tgc ggc caa cag tcc atc cac ttg gga gga gta ttt 967  
 Ser Ser Lys Pro Cys Gly Gln Gln Ser Ile His Leu Gly Gly Val Phe  
 215 220 225

gaa ttg cat cca ggt gct tcg gtg ttc gtc aac gtg act gat cca agc 1015  
 Glu Leu His Pro Gly Ala Ser Val Phe Val Asn Val Thr Asp Pro Ser  
 230 235 240

caa gtg agc cac ggg acc ggc ttc acg tct ttt ggc tta ctc aaa ctc 1063  
 Gln Val Ser His Gly Thr Gly Phe Thr Ser Phe Gly Leu Leu Lys Leu  
 245 250 255 260

tgagtgtgctgg cacctcacag gctgcagctc agctcctgtt ggtgggtcttc gtaatacggc 1123

cgagcagtta agaccaccac ccctgttgaa ctgcctatctt ataaccctag gatcctcctc 1183

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gcggggggcag cgccaacagg ccccggtcgg taagagttga tattctggaa gcagccgccc 1303

cactgatgca gacatccaga gagtcccatg aaaaagacga gactattatg cacagattga 1363

atcctcagta aacggcagat aattagtcca gtttcgtttt gtttctttgc atgcagtgtc 1423

tttcaactgga gaatgtactc gatttccccg cgaagatgct gaagggcaac agggagcctc 1483

agctcacagt cagttacggt tgacccgggg tccccggggc cccgatggag gggacaggct 1543

ccagaaagtc tgatggcgcg gagaactgga aaaccctgcc cccaccagcc accctgacac 1603

tcattctctc cctcctccgc cccctcccc ccacagtcag gctgttgcta atcggttatc 1663

ttatttcaac cctgttgctt ctccaccagt gtaggcggga ggagagagca gaggctgccc 1723

actcctcctc ctgaaatgac tgtattttaa ggaaatctct cctacctacc tgcagtctcc 1783

attgtttcca gagtgaactt gtgattatct tggtatttat tttttgaata ataaagcgcc 1843

cttaacgtta aaaaaaaaaa aaaaaaaaaa aaaaa 1878

<210> 65  
 <211> 260  
 <212> PRT  
 <213> Canis familiaris

<400> 65

Met Ile Glu Thr Tyr Ser Gln Thr Ala Pro Arg Ser Val Ala Thr Gly  
1 5 10 15

Pro Pro Val Ser Met Lys Ile Phe Met Tyr Leu Leu Thr Val Phe Leu  
20 25 30

Ile Thr Gln Met Ile Gly Ser Ala Leu Phe Ala Val Tyr Leu His Arg  
35 40 45

Arg Leu Asp Lys Ile Glu Asp Glu Arg Asn Leu Tyr Glu Asp Phe Val  
50 55 60

Phe Met Lys Thr Leu Gln Lys Cys Asn Lys Gly Glu Gly Ser Leu Ser  
65 70 75 80

Leu Leu Asn Cys Glu Glu Ile Lys Ser Gln Phe Glu Ala Phe Leu Lys  
85 90 95

Glu Ile Met Leu Asn Asn Glu Met Lys Lys Glu Glu Asn Ile Ala Met  
100 105 110

Gln Lys Gly Asp Gln Asp Pro Arg Ile Ala Ala His Val Ile Ser Glu  
115 120 125

Ala Ser Ser Asn Pro Ala Ser Val Leu Arg Trp Ala Pro Lys Gly Tyr  
130 135 140

Tyr Thr Ile Ser Ser Asn Leu Val Ser Leu Glu Asn Gly Lys Gln Leu  
145 150 155 160

Ala Val Lys Arg Gln Gly Leu Tyr Tyr Val Tyr Ala Gln Val Thr Phe  
165 170 175

Cys Ser Asn Arg Ala Ala Ser Ser Gln Ala Pro Phe Val Ala Ser Leu  
180 185 190

Cys Leu His Ser Pro Ser Gly Thr Glu Arg Val Leu Leu Arg Ala Ala  
195 200 205

Ser Ser Arg Gly Ser Ser Lys Pro Cys Gly Gln Gln Ser Ile His Leu  
210 215 220

Gly Gly Val Phe Glu Leu His Pro Gly Ala Ser Val Phe Val Asn Val  
225 230 235 240

Thr Asp Pro Ser Gln Val Ser His Gly Thr Gly Phe Thr Ser Phe Gly



245

250

255

Leu Leu Lys Leu  
260

&lt;210&gt; 66

&lt;211&gt; 1878

&lt;212&gt; DNA

<213> *Canis familiaris*

&lt;400&gt; 66

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taacaagata atcacaagtt cactctggaa acaatggaga ctgcaggtag gtaggagaga 120

tttcctttaa atacagtcac ttcaggagga ggagtgggca gcctctgctc tctcctcccg 180

cctacactgg tggagaggca acaggggtga aataagataa ccgattagca acagcctgac 240

tgtgggggga ggggggcgga ggaggagag aatgagtgtc aggggtggctg gtgggggcag 300

ggttttccag ttctccgcgc catcagactt tctggagcct gtcccctcca tcggggcccc 360

ggggaccccg ggtcaaccgt aactgactgt gagctgaggc tccctgttgc ccttcagcat 420

cttcgcgggg aaatcgagta cattctccag tgaaagacac tgcattgcaa gaaacaaaac 480

gaaactggac taattatctg ccgtttactg aggattcaat ctgtgcataa tagtctcgtc 540

tttttcatgg gactctctgg atgtctgcat cagtggggcg gctgcttcca gaatatcaac 600

tcttaccgac cggggcctgt tggcgtgcc cccgccctgt cattcccttc ttgcagccct 660

ccacgcctgg ggggtgtataa taaatagttc tccacgagga ggatcctagg gttataaata 720

ggcagttcaa caggggtggg ggtcttaact gctcggccgt attacgaaga ccaccaacag 780

gagctgagct gcagcctgtg aggtgccagc actcagagtt tgagtaagcc aaaagacgtg 840

aagccgggtcc cgtggctcac ttggcttggg tcagtcacgt tgacgaacac cgaagcacct 900

ggatgcaatt caaatactcc tccaagtgg atggactgtt ggccgcaagg tttggacgag 960

ccgcgggagc tcgcggcgcg gagtaagact ctctccgttc cactcgggga atggaggcat 1020

aggctggcga cgaacggagc ttgactcgaa gctgcccgat tggagcagaa ggtgacttgg 1080

gcatagacgt aatagagtc tttgtcttttc acggccaact gtttcccatt ctcgaggctc 1140  
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gatcggggag cagtttggct atatgtttcg atcatgctgt gttagagttg aaatgatatc 1620  
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gtcttctctc ccagcaaaaa aagttacgta aaggtttttt tttttttttt tttttttttt 1800  
taattatacc catatcattc acttccaggc tttccctttt gttagtaaag aagaaacaag 1860  
tttcttcttc catacatt 1878

<210> 67  
<211> 780  
<212> DNA  
<213> Canis familiaris

<400> 67  
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ctctttgctg tataatcttca cagaagattg gacaagatag aagatgaaag gaatctttat 180  
gaagattttg tgttcatgaa aacgttacag aaatgcaaca aaggggaggg gtccttgtcc 240  
ttactgaact gtgaggaaat taaaagccaa tttgaagcct ttctcaagga gataatgcta 300  
aacaacgaaa tgaagaaaga agaaaacatt gcaatgcaaa aaggtgatca ggatcctcga 360  
attgcagccc atgtcataag tgaggctagt agtaaccag cgtccgttct gcggtgggcg 420

ccaaaaggggt actacaccat aagcagcaac ctgggtgagcc tcgagaatgg gaaacagttg 480  
 gccgtgaaaa gacaaggact ctattacgtc tatgcccaag tcaccttctg ctccaatcgg 540  
 gcagcttcga gtcaagctcc gttcgtcgcc agcctatgcc tccattcccc gagtggaacg 600  
 gagagagtct tactccgcgc cgcgagctcc cgcggctcgt ccaaaccttg cggccaacag 660  
 tccatccact tgggaggagt atttgaattg catccagggtg cttcgggtgtt cgtcaacgtg 720  
 actgatccaa gccaaagtgag ccacgggacc ggcttcacgt cttttggctt actcaaactc 780

<210> 68

<211> 780

<212> DNA

<213> Canis familiaris

<400> 68

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 cacgttgacg aacaccgaag cacctggatg caattcaaatt actcctccca agtggatgga 120  
 ctggttgccg caaggtttgg acgagccgcg ggagctcgcg gcgcggagta agactctctc 180  
 cgttccactc ggggaatgga ggcataggct ggcgacgaac ggagcttgac tcgaagctgc 240  
 ccgattggag cagaaggtga cttgggcata gacgtaatag agtccttgtc ttttcacggc 300  
 caactgtttc ccattctcga ggctcaccag gttgctgctt atgggtgtagt acccttttgg 360  
 cgcccaccgc agaacggacg ctgggttact actagcctca cttatgacat gggctgcaat 420  
 tcgaggatcc tgatcacctt tttgcattgc aatgttttct tctttcttca tttcgttggt 480  
 tagcattatc tccttgagaa aggcctcaaa ttggctttta atttcctcac agttcagtaa 540  
 ggacaaggac ccctcccctt tgttgcattt ctgtaacgtt ttcataaaca caaaatcttc 600  
 ataaagattc ctttcatctt ctatcttgtc caatcttctg tgaagatata cagcaaagag 660  
 tgccgatcca atcatctggg tgatgagaaa aacagtaagc aaatacataa aaattttcat 720  
 actgacgggt ggtccagtgg ccacagatcg gggagcagtt tggctatatg tttcgatcat 780

<210> 69

<211> 633  
 <212> DNA  
 <213> Canis familiaris

<220>  
 <221> CDS  
 <222> (1)..(633)

<400> 69  
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 Leu Asp Lys Ile Glu Asp Glu Arg Asn Leu Tyr Glu Asp Phe Val Phe  
 1 5 10 15  
 atg aaa acg tta cag aaa tgc aac aaa ggg gag ggg tcc ttg tcc tta 96  
 Met Lys Thr Leu Gln Lys Cys Asn Lys Gly Glu Gly Ser Leu Ser Leu  
 20 25 30  
 ctg aac tgt gag gaa att aaa agc caa ttt gaa gcc ttt ctc aag gag 144  
 Leu Asn Cys Glu Glu Ile Lys Ser Gln Phe Glu Ala Phe Leu Lys Glu  
 35 40 45  
 ata atg cta aac aac gaa atg aag aaa gaa gaa aac att gca atg caa 192  
 Ile Met Leu Asn Asn Glu Met Lys Lys Glu Glu Asn Ile Ala Met Gln  
 50 55 60  
 aaa ggt gat cag gat cct cga att gca gcc cat gtc ata agt gag gct 240  
 Lys Gly Asp Gln Asp Pro Arg Ile Ala Ala His Val Ile Ser Glu Ala  
 65 70 75 80  
 agt agt aac cca gcg tcc gtt ctg cgg tgg gcg cca aaa ggg tac tac 288  
 Ser Ser Asn Pro Ala Ser Val Leu Arg Trp Ala Pro Lys Gly Tyr Tyr  
 85 90 95  
 acc ata agc agc aac ctg gtg agc ctc gag aat ggg aaa cag ttg gcc 336  
 Thr Ile Ser Ser Asn Leu Val Ser Leu Glu Asn Gly Lys Gln Leu Ala  
 100 105 110  
 gtg aaa aga caa gga ctc tat tac gtc tat gcc caa gtc acc ttc tgc 384  
 Val Lys Arg Gln Gly Leu Tyr Tyr Val Tyr Ala Gln Val Thr Phe Cys  
 115 120 125  
 tcc aat cgg gca gct tcg agt caa gct ccg ttc gtc gcc agc cta tgc 432  
 Ser Asn Arg Ala Ala Ser Ser Gln Ala Pro Phe Val Ala Ser Leu Cys  
 130 135 140  
 ctc cat tcc ccg agt gga acg gag aga gtc tta ctc cgc gcc gcg agc 480  
 Leu His Ser Pro Ser Gly Thr Glu Arg Val Leu Leu Arg Ala Ala Ser  
 145 150 155 160

tcc cgc ggc tcg tcc aaa cct tgc ggc caa cag tcc atc cac ttg gga	528
Ser Arg Gly Ser Ser Lys Pro Cys Gly Gln Gln Ser Ile His Leu Gly	
165 170 175	

gga gta ttt gaa ttg cat cca ggt gct tcg gtg ttc gtc aac gtg act	576
Gly Val Phe Glu Leu His Pro Gly Ala Ser Val Phe Val Asn Val Thr	
180 185 190	

gat cca agc caa gtg agc cac ggg acc ggc ttc acg tct ttt ggc tta	624
Asp Pro Ser Gln Val Ser His Gly Thr Gly Phe Thr Ser Phe Gly Leu	
195 200 205	

ctc aaa ctc	633
Leu Lys Leu	
210	

<210> 70  
 <211> 211  
 <212> PRT  
 <213> Canis familiaris

<400> 70	
Leu Asp Lys Ile Glu Asp Glu Arg Asn Leu Tyr Glu Asp Phe Val Phe	
1 5 10 15	

Met Lys Thr Leu Gln Lys Cys Asn Lys Gly Glu Gly Ser Leu Ser Leu	
20 25 30	

Leu Asn Cys Glu Glu Ile Lys Ser Gln Phe Glu Ala Phe Leu Lys Glu	
35 40 45	

Ile Met Leu Asn Asn Glu Met Lys Lys Glu Glu Asn Ile Ala Met Gln	
50 55 60	

Lys Gly Asp Gln Asp Pro Arg Ile Ala Ala His Val Ile Ser Glu Ala	
65 70 75 80	

Ser Ser Asn Pro Ala Ser Val Leu Arg Trp Ala Pro Lys Gly Tyr Tyr	
85 90 95	

Thr Ile Ser Ser Asn Leu Val Ser Leu Glu Asn Gly Lys Gln Leu Ala	
100 105 110	

Val Lys Arg Gln Gly Leu Tyr Tyr Val Tyr Ala Gln Val Thr Phe Cys	
115 120 125	

Ser Asn Arg Ala Ala Ser Ser Gln Ala Pro Phe Val Ala Ser Leu Cys  
 130 135 140

Leu His Ser Pro Ser Gly Thr Glu Arg Val Leu Leu Arg Ala Ala Ser  
 145 150 155 160

Ser Arg Gly Ser Ser Lys Pro Cys Gly Gln Gln Ser Ile His Leu Gly  
 165 170 175

Gly Val Phe Glu Leu His Pro Gly Ala Ser Val Phe Val Asn Val Thr  
 180 185 190

Asp Pro Ser Gln Val Ser His Gly Thr Gly Phe Thr Ser Phe Gly Leu  
 195 200 205

Leu Lys Leu  
 210

<210> 71

<211> 633

<212> DNA

<213> Canis familiaris

<400> 71

gagtttgagt aagccaaaag acgtgaagcc ggtcccgtgg ctcaattggc ttggatcagt 60

cacgttgacg aacaccgaag cacctggatg caattcaaact actcctccca agtggatgga 120

ctgttggccg caaggtttgg acgagccgcg ggagctcgcg gcgcggagta agactctctc 180

cgttccactc ggggaatgga ggcataaggct ggcgacgaac ggagcttgac tcgaagctgc 240

ccgattggag cagaaggtga cttgggcata gacgtaatag agtccttgtc ttttcacggc 300

caactgtttc ccattctcga ggctcaccag gttgctgctt atggtgtagt acccttttgg 360

cgcccaccgc agaacggacg ctgggttact actagcctca cttatgacat gggctgcaat 420

tcgaggatcc tgatcacctt tttgcattgc aatgttttct tctttcttca tttcgttggt 480

tagcattatc tccttgagaa aggcttcaaa ttggctttta atttcctcac agttcagtaa 540

ggacaaggac ccctcccctt tgttgcattt ctgtaacgtt ttcatagaaca caaaatcttc 600

ataaagattc ctttcatctt ctatcttgtc caa 633

<210> 72  
 <211> 885  
 <212> DNA  
 <213> Felis catus

<220>  
 <221> CDS  
 <222> (29)..(808)

<400> 72

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                          1                      5

gct ccc cgc tcc gtg gcc cct gga cca ccc gtc agt atg aaa att ttt      100
Ala Pro Arg Ser Val Ala Pro Gly Pro Pro Val Ser Met Lys Ile Phe
      10                      15                      20

atg tat tta ctt act gtg ttt ctc atc acc cag atg att ggg tca gca      148
Met Tyr Leu Leu Thr Val Phe Leu Ile Thr Gln Met Ile Gly Ser Ala
      25                      30                      35                      40

ctc ttt gct gtg tat ctt cac aga aga ctg gac aag ata gaa gat gaa      196
Leu Phe Ala Val Tyr Leu His Arg Arg Leu Asp Lys Ile Glu Asp Glu
                        45                      50                      55

agg aat ctt tat gaa gat ttt gtg ttc atg aaa aca tta cag aaa tgc      244
Arg Asn Leu Tyr Glu Asp Phe Val Phe Met Lys Thr Leu Gln Lys Cys
                        60                      65                      70

aac aaa gga gag ggg gcc tta tcc tta ctg aac tgt gag gaa att aaa      292
Asn Lys Gly Glu Gly Ala Leu Ser Leu Leu Asn Cys Glu Glu Ile Lys
                        75                      80                      85

agc cgg ttt gaa gcc ttt ctc aag gag ata atg cta aac aaa gaa acg      340
Ser Arg Phe Glu Ala Phe Leu Lys Glu Ile Met Leu Asn Lys Glu Thr
                        90                      95                      100

aag aaa gaa aaa aat gtt gca atg caa aaa ggc gac cag gat cct cga      388
Lys Lys Glu Lys Asn Val Ala Met Gln Lys Gly Asp Gln Asp Pro Arg
      105                      110                      115                      120

gtt gca gca cat gtc ata agt gag gcc agc agt agc aca gcg tct gtt      436
Val Ala Ala His Val Ile Ser Glu Ala Ser Ser Ser Thr Ala Ser Val
                        125                      130                      135

ctc cag tgg gcc ccc aaa ggc tac tac acc ata agc agc aac ttg gtg      484
Leu Gln Trp Ala Pro Lys Gly Tyr Tyr Thr Ile Ser Ser Asn Leu Val

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140	145	150	
acc ctc gag aac ggg aag cag ctg gcc gtt aaa aga caa gga ctc tat	532		
Thr Leu Glu Asn Gly Lys Gln Leu Ala Val Lys Arg Gln Gly Leu Tyr			
155	160	165	
tat atc tac gcc caa gtc acc ttc tgt tcc aat cgg gaa gct tcg agt	580		
Tyr Ile Tyr Ala Gln Val Thr Phe Cys Ser Asn Arg Glu Ala Ser Ser			
170	175	180	
caa gct ccg ttc ata gcc agc ctc tgc ctg cat tcc ccg agt gga tcc	628		
Gln Ala Pro Phe Ile Ala Ser Leu Cys Leu His Ser Pro Ser Gly Ser			
185	190	195	200
gag aga gtc tta ctc aga gct gca aat gcc cgc agt tcc tcc aaa ccc	676		
Glu Arg Val Leu Leu Arg Ala Ala Asn Ala Arg Ser Ser Ser Lys Pro			
205	210	215	
tgt ggg cag caa tcc att cac ttg gga gga gtc ttc gaa ctg cat cca	724		
Cys Gly Gln Gln Ser Ile His Leu Gly Gly Val Phe Glu Leu His Pro			
220	225	230	
ggt gct tcg gtg ttc gtg aac gtg act gat ccg agc caa gtg agc cac	772		
Gly Ala Ser Val Phe Val Asn Val Thr Asp Pro Ser Gln Val Ser His			
235	240	245	
ggg acg ggc ttc acg tct ttt ggc ttg ctc aaa ctc tgaacactgg	818		
Gly Thr Gly Phe Thr Ser Phe Gly Leu Leu Lys Leu			
250	255	260	
cacctcgcag gccgcgaggc ctgcaggccg cggctgagct cacgctggga gtcttcacaa	878		
tacagca	885		

<210> 73  
 <211> 260  
 <212> PRT  
 <213> Felis catus

<400> 73  
 Met Ile Glu Thr Tyr Ser Gln Thr Ala Pro Arg Ser Val Ala Pro Gly  
 1 5 10 15  
 Pro Pro Val Ser Met Lys Ile Phe Met Tyr Leu Leu Thr Val Phe Leu  
 20 25 30  
 Ile Thr Gln Met Ile Gly Ser Ala Leu Phe Ala Val Tyr Leu His Arg



35					40					45						
Arg	Leu	Asp	Lys	Ile	Glu	Asp	Glu	Arg	Asn	Leu	Tyr	Glu	Asp	Phe	Val	
50					55					60						
Phe	Met	Lys	Thr	Leu	Gln	Lys	Cys	Asn	Lys	Gly	Glu	Gly	Ala	Leu	Ser	
65					70					75					80	
Leu	Leu	Asn	Cys	Glu	Glu	Ile	Lys	Ser	Arg	Phe	Glu	Ala	Phe	Leu	Lys	
85					90					95						
Glu	Ile	Met	Leu	Asn	Lys	Glu	Thr	Lys	Lys	Glu	Lys	Asn	Val	Ala	Met	
100					105					110						
Gln	Lys	Gly	Asp	Gln	Asp	Pro	Arg	Val	Ala	Ala	His	Val	Ile	Ser	Glu	
115					120					125						
Ala	Ser	Ser	Ser	Thr	Ala	Ser	Val	Leu	Gln	Trp	Ala	Pro	Lys	Gly	Tyr	
130					135					140						
Tyr	Thr	Ile	Ser	Ser	Asn	Leu	Val	Thr	Leu	Glu	Asn	Gly	Lys	Gln	Leu	
145					150					155					160	
Ala	Val	Lys	Arg	Gln	Gly	Leu	Tyr	Tyr	Ile	Tyr	Ala	Gln	Val	Thr	Phe	
165					170					175						
Cys	Ser	Asn	Arg	Glu	Ala	Ser	Ser	Gln	Ala	Pro	Phe	Ile	Ala	Ser	Leu	
180					185					190						
Cys	Leu	His	Ser	Pro	Ser	Gly	Ser	Glu	Arg	Val	Leu	Leu	Arg	Ala	Ala	
195					200					205						
Asn	Ala	Arg	Ser	Ser	Ser	Lys	Pro	Cys	Gly	Gln	Gln	Ser	Ile	His	Leu	
210					215					220						
Gly	Gly	Val	Phe	Glu	Leu	His	Pro	Gly	Ala	Ser	Val	Phe	Val	Asn	Val	
225					230					235					240	
Thr	Asp	Pro	Ser	Gln	Val	Ser	His	Gly	Thr	Gly	Phe	Thr	Ser	Phe	Gly	
245					250					255						
Leu	Leu	Lys	Leu													
260																

<210> 74  
 <211> 885  
 <212> DNA

<213> Felis catus

<400> 74

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acttggctcg gatcagtcac gttcacgaac accgaagcac ctggatgcag ttcgaagact 180  
cctcccaagt gaatggattg ctgcccacag ggtttgaggg aactgcgggc atttgcagct 240  
ctgagtaaga ctctctcgga tccactcggg gaatgcaggc agaggctggc tatgaacgga 300  
gcttgactcg aagcttcccg attggaacag aagggtgactt gggcgtagat ataataagagt 360  
ccttgtcttt taacggccag ctgcttcccg ttctcgaggg tcaccaagtt gctgcttatg 420  
gtgtagtagc ctttgggggc ccaactggaga acagacgctg tgctactgct ggcctcactt 480  
atgacatgtg ctgcaactcg aggatcctgg tcgccttttt gcattgcaac atttttttct 540  
ttcttcgttt ctttgttttag cattatctcc ttgagaaagg cttcaaaccg gctttttaatt 600  
tcctcacagt tcagtaagga taaggccccc tctcctttgt tgcatttctg taatgttttc 660  
atgaacacaa aatcttcata aagattcctt tcattcttcta tcttgtccag tcttctgtga 720  
agatacacag caaagagtgc tgaccaatc atctgggtga tgagaaacac agtaagtaaa 780  
tacataaaaa ttttcatact gacgggtggt ccaggggcca cggagcgggg agcagtttgg 840  
ctatatgttt cgatcatgct gtgttaaagt tgaaatggta tcttc 885

<210> 75

<211> 780

<212> DNA

<213> Felis catus

<400> 75

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ctctttgctg tgtatcttca cagaagactg gacaagatag aagatgaaag gaatctttat 180  
gaagattttg tgttcatgaa aacattacag aaatgcaaca aaggagaggg ggccttatcc 240

ttactgaact gtgaggaaat taaaagccgg tttgaagcct ttctcaagga gataatgcta 300  
 aacaaagaaa cgaagaaaga aaaaaatggt gcaatgcaaa aaggcgacca ggatcctcga 360  
 gttgcagcac atgtcataag tgaggccagc agtagcacag cgtctgttct ccagtgggcc 420  
 cccaaaggct actacaccat aagcagcaac ttggtgaccc tcgagaacgg gaagcagctg 480  
 gccgttaaaa gacaaggact ctattatatac tacgccaag tcaccttctg ttccaatcgg 540  
 gaagcttcga gtcaagctcc gttcatagcc agcctctgcc tgcattcccc gagtggatcc 600  
 gagagagtct tactcagagc tgcaaagtcc cgcagttcct ccaaaccctg tgggcagcaa 660  
 tccattcact tgggaggagt cttcgaactg catccagggtg cttcgggtgtt cgtgaacgtg 720  
 actgatccga gccaaagtga ccacgggacg ggcttcacgt cttttggctt gctcaaactc 780

<210> 76  
 <211> 780  
 <212> DNA  
 <213> Felis catus

<400> 76  
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 ttgctgcca cagggtttgg aggaactgcg ggcatttgca gctctgagta agactctctc 180  
 ggatccactc ggggaatgca ggcagaggct ggctatgaac ggagcttgac tcgaagcttc 240  
 ccgattggaa cagaagggtga cttgggcgta gatataatag agtccttgtc ttttaacggc 300  
 cagctgcttc ccgttctcga gggtcaccaa gttgctgctt atgggtgtagt agcctttggg 360  
 ggcccactgg agaacagacg ctgtgctact gctggcctca cttatgacat gtgctgcaac 420  
 tcgaggatcc tggtcgcctt tttgcattgc aacatttttt tctttcttcg tttctttgtt 480  
 tagcattatc tccttgagaa aggcttcaaa ccggctttta atttcctcac agttcagtaa 540  
 ggataaggcc ccctctcctt tggtgcattt ctgtaatggt ttcattgaaca caaatcttc 600  
 ataaagattc ctttcatctt ctatcttgtc cagtcttctg tgaagataca cagcaaagag 660  
 tgctgacca atcatctggg tgatgagaaa cacagtaagt aaatacataa aaattttcat 720

actgacgggt ggtccagggg ccacggagcg gggagcagtt tggctatatg tttcgatcat 780

<210> 77

<211> 633

<212> DNA

<213> Felis catus

<220>

<221> CDS

<222> (1)..(633)

<400> 77

ctg gac aag ata gaa gat gaa agg aat ctt tat gaa gat ttt gtg ttc	48
Leu Asp Lys Ile Glu Asp Glu Arg Asn Leu Tyr Glu Asp Phe Val Phe	
1 5 10 15	

atg aaa aca tta cag aaa tgc aac aaa gga gag ggg gcc tta tcc tta	96
Met Lys Thr Leu Gln Lys Cys Asn Lys Gly Glu Gly Ala Leu Ser Leu	
20 25 30	

ctg aac tgt gag gaa att aaa agc cgg ttt gaa gcc ttt ctc aag gag	144
Leu Asn Cys Glu Glu Ile Lys Ser Arg Phe Glu Ala Phe Leu Lys Glu	
35 40 45	

ata atg cta aac aaa gaa acg aag aaa gaa aaa aat gtt gca atg caa	192
Ile Met Leu Asn Lys Glu Thr Lys Lys Glu Lys Asn Val Ala Met Gln	
50 55 60	

aaa ggc gac cag gat cct cga gtt gca gca cat gtc ata agt gag gcc	240
Lys Gly Asp Gln Asp Pro Arg Val Ala Ala His Val Ile Ser Glu Ala	
65 70 75 80	

agc agt agc aca gcg tct gtt ctc cag tgg gcc ccc aaa ggc tac tac	288
Ser Ser Ser Thr Ala Ser Val Leu Gln Trp Ala Pro Lys Gly Tyr Tyr	
85 90 95	

acc ata agc agc aac ttg gtg acc ctc gag aac ggg aag cag ctg gcc	336
Thr Ile Ser Ser Asn Leu Val Thr Leu Glu Asn Gly Lys Gln Leu Ala	
100 105 110	

gtt aaa aga caa gga ctc tat tat atc tac gcc caa gtc acc ttc tgt	384
Val Lys Arg Gln Gly Leu Tyr Tyr Ile Tyr Ala Gln Val Thr Phe Cys	
115 120 125	

tcc aat cgg gaa gct tcg agt caa gct ccg ttc ata gcc agc ctc tgc	432
Ser Asn Arg Glu Ala Ser Ser Gln Ala Pro Phe Ile Ala Ser Leu Cys	

130	135	140	
ctg cat tcc ccg agt gga tcc gag aga gtc tta ctc aga gct gca aat	480		
Leu His Ser Pro Ser Gly Ser Glu Arg Val Leu Leu Arg Ala Ala Asn			
145	150	155	160
gcc cgc agt tcc tcc aaa ccc tgt ggg cag caa tcc att cac ttg gga	528		
Ala Arg Ser Ser Ser Lys Pro Cys Gly Gln Gln Ser Ile His Leu Gly			
165	170	175	
gga gtc ttc gaa ctg cat cca ggt gct tcg gtg ttc gtg aac gtg act	576		
Gly Val Phe Glu Leu His Pro Gly Ala Ser Val Phe Val Asn Val Thr			
180	185	190	
gat ccg agc caa gtg agc cac ggg acg ggc ttc acg tct ttt ggc ttg	624		
Asp Pro Ser Gln Val Ser His Gly Thr Gly Phe Thr Ser Phe Gly Leu			
195	200	205	
ctc aaa ctc	633		
Leu Lys Leu			
210			
<210> 78			
<211> 211			
<212> PRT			
<213> Felis catus			
<400> 78			
Leu Asp Lys Ile Glu Asp Glu Arg Asn Leu Tyr Glu Asp Phe Val Phe			
1	5	10	15
Met Lys Thr Leu Gln Lys Cys Asn Lys Gly Glu Gly Ala Leu Ser Leu			
20	25	30	
Leu Asn Cys Glu Glu Ile Lys Ser Arg Phe Glu Ala Phe Leu Lys Glu			
35	40	45	
Ile Met Leu Asn Lys Glu Thr Lys Lys Glu Lys Asn Val Ala Met Gln			
50	55	60	
Lys Gly Asp Gln Asp Pro Arg Val Ala Ala His Val Ile Ser Glu Ala			
65	70	75	80
Ser Ser Ser Thr Ala Ser Val Leu Gln Trp Ala Pro Lys Gly Tyr Tyr			
85	90	95	
Thr Ile Ser Ser Asn Leu Val Thr Leu Glu Asn Gly Lys Gln Leu Ala			

100	105	110
Val Lys Arg Gln Gly Leu Tyr Tyr Ile Tyr Ala Gln Val Thr Phe Cys		
115	120	125
Ser Asn Arg Glu Ala Ser Ser Gln Ala Pro Phe Ile Ala Ser Leu Cys		
130	135	140
Leu His Ser Pro Ser Gly Ser Glu Arg Val Leu Leu Arg Ala Ala Asn		
145	150	155
Ala Arg Ser Ser Ser Lys Pro Cys Gly Gln Gln Ser Ile His Leu Gly		
165	170	175
Gly Val Phe Glu Leu His Pro Gly Ala Ser Val Phe Val Asn Val Thr		
180	185	190
Asp Pro Ser Gln Val Ser His Gly Thr Gly Phe Thr Ser Phe Gly Leu		
195	200	205
Leu Lys Leu		
210		

<210> 79  
 <211> 633  
 <212> DNA  
 <213> Felis catus

<400> 79  
 gagtttgagc aagccaaaag acgtgaagcc cgtcccgtgg ctcaactggc tcggatcagt 60  
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 ttgctgcca cagggtttgg aggaactgcg ggcatttgca gctctgagta agactctctc 180  
 ggatccactc ggggaatgca ggcagaggct ggctatgaac ggagcttgac tcgaagcttc 240  
 ccgattggaa cagaagggtga cttggggcgta gatataatag agtccttgctc ttttaacggc 300  
 cagctgcttc ccgttctcga gggtcaccaa gttgctgctt atgggtgtagt agcctttggg 360  
 ggcccactgg agaacagacg ctgtgctact gctggcctca cttatgacat gtgctgcaac 420  
 tcgaggatcc tggtcgcctt tttgcattgc aacatTTTTT tctttcttcg tttctttggt 480  
 tagcattatc tccttgagaa aggcttcaaa ccggctttta atttcctcac agttcagtaa 540

ggataaggcc ccctctcctt tggtgcattt ctgtaatggt ttcataaaca caaaatcttc 600

ataaagattc ctttcatctt ctatcttgtc cag 633

<210> 80

<211> 610

<212> DNA

<213> Canis familiaris

<220>

<221> CDS

<222> (29)..(430)

<400> 80

caaggcaaac actgaacatt tcagagct atg aga atg ctt ctg aat ttg agt 52  
Met Arg Met Leu Leu Asn Leu Ser  
1 5

ttg cta gct ctt ggg gct gcc tat gtt tct gcc ttt gct gta gaa aat 100  
Leu Leu Ala Leu Gly Ala Ala Tyr Val Ser Ala Phe Ala Val Glu Asn  
10 15 20

ccc atg aat aga ctg gtg gca gag acc ttg aca ctg ctc tcc act cat 148  
Pro Met Asn Arg Leu Val Ala Glu Thr Leu Thr Leu Leu Ser Thr His  
25 30 35 40

cga act tgg ctg ata ggc gat ggg aac ctg atg att cct act cct gaa 196  
Arg Thr Trp Leu Ile Gly Asp Gly Asn Leu Met Ile Pro Thr Pro Glu  
45 50 55

aat aaa aat cac caa ctg tgc att aaa gaa gtt ttt cag ggt ata gac 244  
Asn Lys Asn His Gln Leu Cys Ile Lys Glu Val Phe Gln Gly Ile Asp  
60 65 70

aca ttg aag aac caa act gcc cac ggg gag gct gtg gat aaa cta ttc 292  
Thr Leu Lys Asn Gln Thr Ala His Gly Glu Ala Val Asp Lys Leu Phe  
75 80 85

caa aac ttg tct tta ata aaa gaa cac ata gag cgc caa aaa aaa agg 340  
Gln Asn Leu Ser Leu Ile Lys Glu His Ile Glu Arg Gln Lys Lys Arg  
90 95 100

tgt gca gga gaa aga tgg aga gtg aca aag ttc cta gac tac ctg caa 388  
Cys Ala Gly Glu Arg Trp Arg Val Thr Lys Phe Leu Asp Tyr Leu Gln  
105 110 115 120

gta ttt ctt ggt gta ata aac acc gag tgg aca ccg gaa agt 430

Val Phe Leu Gly Val Ile Asn Thr Glu Trp Thr Pro Glu Ser  
125 130

tgagaacaaa ccggcttatt gtagtggaag attttggaaga agaatgggttt tttggcgatg 490  
agaatgaggg ccaaccaaca gtagggactt aatggccagt ataactaagc ttcagagaca 550  
aagtaaatat ttcaggcatc ctactacttt atcacttcac acagatgaaa tatatttgag 610

<210> 81  
<211> 134  
<212> PRT  
<213> Canis familiaris

<400> 81  
Met Arg Met Leu Leu Asn Leu Ser Leu Leu Ala Leu Gly Ala Ala Tyr  
1 5 10 15  
Val Ser Ala Phe Ala Val Glu Asn Pro Met Asn Arg Leu Val Ala Glu  
20 25 30  
Thr Leu Thr Leu Leu Ser Thr His Arg Thr Trp Leu Ile Gly Asp Gly  
35 40 45  
Asn Leu Met Ile Pro Thr Pro Glu Asn Lys Asn His Gln Leu Cys Ile  
50 55 60  
Lys Glu Val Phe Gln Gly Ile Asp Thr Leu Lys Asn Gln Thr Ala His  
65 70 75 80  
Gly Glu Ala Val Asp Lys Leu Phe Gln Asn Leu Ser Leu Ile Lys Glu  
85 90 95  
His Ile Glu Arg Gln Lys Lys Arg Cys Ala Gly Glu Arg Trp Arg Val  
100 105 110  
Thr Lys Phe Leu Asp Tyr Leu Gln Val Phe Leu Gly Val Ile Asn Thr  
115 120 125  
Glu Trp Thr Pro Glu Ser  
130

<210> 82  
<211> 610  
<212> DNA  
<213> Canis familiaris



<400> 82

ctcaaata tttcatctgt gtgaagtgat aaagtagtag gatgcctgaa atatttactt 60  
tgtctctgaa gcttagttat actggccatt aagtccttac tgttggttgg ccctcattct 120  
catcgccaaa aaaccattct tctccaaaat cttccactac aataagccgg tttgttctca 180  
actttccggg gtccactcgg tgtttattac accaagaaat acttgcagg agtctaggaa 240  
ctttgtcact ctccatcttt ctctgcaca cttttttttt tggcgctcta tgtgttcttt 300  
tattaaagac aagttttgga atagtttata cacagcctcc ccgtgggcag tttggttctt 360  
caatgtgtct ataccctgaa aaacttcttt aatgcacagt tgggtgatttt tattttcagg 420  
agtaggaatc atcaggttcc catcgcttat cagccaagtt cgatgagtgg agagcagtgt 480  
caaggtctct gccaccagtc tattcatggg attttctaca gcaaaggcag aaacataggc 540  
agccccaaga gctagcaaac tcaaattcag aagcattctc atagctctga aatgttcagt 600  
gtttgccttg 610

<210> 83

<211> 402

<212> DNA

<213> Canis familiaris

<400> 83

atgagaatgc ttctgaattt gagtttgcta gctcttgggg ctgcctatgt ttctgccttt 60  
gctgtagaaa atcccatgaa tagactgggt gcagagacct tgacactgct ctccactcat 120  
cgaacttggc tgataggcga tgggaacctg atgattccta ctctgaaaa taaaaatcac 180  
caactgtgca ttaaagaagt ttttcagggt atagacacat tgaagaacca aactgcccac 240  
ggggaggctg tggataaact attccaaaac ttgtctttta taaaagaaca catagagcgc 300  
caaaaaaaaaa ggtgtgcagg agaaagatgg agagtgacaa agttcctaga ctacctgcaa 360  
gtatttcttg gtgtaataaa caccgagtgg acaccggaaa gt 402

<210> 84

<211> 402

<212> DNA  
 <213> Canis familiaris

<400> 84  
 actttccggt gtccactcgg tgtttattac accaagaaat acttgcaggt agtctaggaa 60  
 ctttgtcact ctccatcttt ctctgcaca cttttttttt tggcgctcta tgtgttcttt 120  
 tattaaagac aagttttgga atagtttata cacagcctcc ccgtgggcag tttggttctt 180  
 caatgtgtct ataccctgaa aaacttcttt aatgcacagt tgggtgatttt tattttcagg 240  
 agtaggaatc atcaggttcc catcgccctat cagccaagtt cgatgagtgg agagcagtgt 300  
 caaggtctct gccaccagtc tattcatggg attttctaca gcaaaggcag aaacataggc 360  
 agccccaaga gctagcaaac tcaaattcag aagcattctc at 402

<210> 85  
 <211> 345  
 <212> DNA  
 <213> Canis familiaris

<220>  
 <221> CDS  
 <222> (1)..(345)

<400> 85  
 ttt gct gta gaa aat ccc atg aat aga ctg gtg gca gag acc ttg aca 48  
 Phe Ala Val Glu Asn Pro Met Asn Arg Leu Val Ala Glu Thr Leu Thr  
 1 5 10 15  
 ctg ctc tcc act cat cga act tgg ctg ata ggc gat ggg aac ctg atg 96  
 Leu Leu Ser Thr His Arg Thr Trp Leu Ile Gly Asp Gly Asn Leu Met  
 20 25 30  
 att cct act cct gaa aat aaa aat cac caa ctg tgc att aaa gaa gtt 144  
 Ile Pro Thr Pro Glu Asn Lys Asn His Gln Leu Cys Ile Lys Glu Val  
 35 40 45  
 ttt cag ggt ata gac aca ttg aag aac caa act gcc cac ggg gag gct 192  
 Phe Gln Gly Ile Asp Thr Leu Lys Asn Gln Thr Ala His Gly Glu Ala  
 50 55 60  
 gtg gat aaa cta ttc caa aac ttg tct tta ata aaa gaa cac ata gag 240  
 Val Asp Lys Leu Phe Gln Asn Leu Ser Leu Ile Lys Glu His Ile Glu  
 65 70 75 80

cgc caa aaa aaa agg tgt gca gga gaa aga tgg aga gtg aca aag ttc 288  
 Arg Gln Lys Lys Arg Cys Ala Gly Glu Arg Trp Arg Val Thr Lys Phe  
                   85                                  90                                  95

cta gac tac ctg caa gta ttt ctt ggt gta ata aac acc gag tgg aca 336  
 Leu Asp Tyr Leu Gln Val Phe Leu Gly Val Ile Asn Thr Glu Trp Thr  
                   100                                  105                                  110

ccg gaa agt 345  
 Pro Glu Ser  
           115

<210> 86  
 <211> 115  
 <212> PRT  
 <213> Canis familiaris

<400> 86  
 Phe Ala Val Glu Asn Pro Met Asn Arg Leu Val Ala Glu Thr Leu Thr  
   1                                  5                                  10                                  15

Leu Leu Ser Thr His Arg Thr Trp Leu Ile Gly Asp Gly Asn Leu Met  
                   20                                  25                                  30

Ile Pro Thr Pro Glu Asn Lys Asn His Gln Leu Cys Ile Lys Glu Val  
                   35                                  40                                  45

Phe Gln Gly Ile Asp Thr Leu Lys Asn Gln Thr Ala His Gly Glu Ala  
           50                                  55                                  60

Val Asp Lys Leu Phe Gln Asn Leu Ser Leu Ile Lys Glu His Ile Glu  
   65                                  70                                  75                                  80

Arg Gln Lys Lys Arg Cys Ala Gly Glu Arg Trp Arg Val Thr Lys Phe  
                   85                                  90                                  95

Leu Asp Tyr Leu Gln Val Phe Leu Gly Val Ile Asn Thr Glu Trp Thr  
                   100                                  105                                  110

Pro Glu Ser  
           115

<210> 87  
 <211> 345  
 <212> DNA

<213> Canis familiaris

<400> 87

actttccggt gtccactcgg tgtttattac accaagaaat acttgcaggt agtctaggaa 60  
ctttgtcact ctccatcttt ctctgcaca cctttttttt tggcgctcta tgtgttcttt 120  
tattaaagac aagttttgga atagtttata cacagcctcc ccgtgggcag ttgggttctt 180  
caatgtgtct ataccctgaa aaacttcttt aatgcacagt tgggtatttt tattttcagg 240  
agtaggaatc atcaggttcc catcgcttat cagccaagtt cgatgagtgg agagcagtgt 300  
caaggtctct gccaccagtc tattcatggg attttctaca gcaaa 345

<210> 88

<211> 166

<212> DNA

<213> Canis familiaris

<400> 88

ctcagcttag gccagcctac gacctgcctg ctcttccctc gtcctcctg cattggctct 60  
gggctccatg gcgctctggt tgactgtggt cattgctctc acctgcctcg gtggccttgc 120  
ctccccgagc cctgtgactc cctccccaac cctcaaggag ctcat 166

<210> 89

<211> 272

<212> DNA

<213> Canis familiaris

<400> 89

tggccttgcc tccccgagcc ctgtgactcc ctccccaacc ctcaaggagc tcattgagga 60  
gctggtcaac atcaccaga atcaggcatc cctctgcaac ggcagcatgg tgtggagcgt 120  
caacctgacc gccggcatgt actgcgcagc tctagaatct ctgatcaatg tctccgactg 180  
cagcgccatc caaaggaccc agaggatgct gaaagcactg tgctctcaaa agcccgcggc 240  
agggcagatt tccagtgaac gcagccgaga ca 272

<210> 90

<211> 278

<212> DNA  
<213> Canis familiaris

<400> 90  
atggcgctct ggttgactgt ggtcattgct ctcacctgcc tcggtggcct tgccctccccg 60  
agccctgtga ctccctcccc aacctcaag gagctcattg aggagctggt caacatcacc 120  
cagaatcagg catccctctg caacggcagc atggtgtgga gcgtaaacct gaccgccggc 180  
atgtactgcg cagctctaga atctctgatc aatgtctccg actgcagcgc catccaaagg 240  
accagagga tgctgaaagc actgtgctct caaaagcc 278

<210> 91  
<211> 1302  
<212> DNA  
<213> Canis familiaris

<220>  
<221> CDS  
<222> (52)..(444)

<400> 91  
ctacgacctg cctgctcttc cctcgctcct cctgcattgg ctctgggctc c atg gcg 57  
Met Ala  
1  
  
ctc tgg ttg act gtg gtc att gct ctc acc tgc ctc ggt ggc ctt gcc 105  
Leu Trp Leu Thr Val Val Ile Ala Leu Thr Cys Leu Gly Gly Leu Ala  
5 10 15  
  
tcc ccg agc cct gtg act ccc tcc cca acc ctc aag gag ctc att gag 153  
Ser Pro Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu Ile Glu  
20 25 30  
  
gag ctg gtc aac atc acc cag aat cag gca tcc ctc tgc aac ggc agc 201  
Glu Leu Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn Gly Ser  
35 40 45 50  
  
atg gtg tgg agc gtc aac ctg acc gcc ggc atg tac tgc gca gct cta 249  
Met Val Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala Leu  
55 60 65  
  
gaa tct ctg atc aat gtc tcc gac tgc agc gcc atc caa agg acc cag 297  
Glu Ser Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg Thr Gln  
70 75 80

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agg atg ctg aaa gca ctg tgc tct caa aag ccc gcg gca ggg cag att 345
Arg Met Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly Gln Ile
      85                      90                      95

tcc agt gaa cgc agc cga gac acc aaa att gaa gtg atc cag ttg gtg 393
Ser Ser Glu Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln Leu Val
    100                      105                      110

aaa aac ctg ctc acc tat gta agg gga gtt tat cgc cat gga aat ttc 441
Lys Asn Leu Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly Asn Phe
115                      120                      125                      130

aga tgaagcatga aaacttagca tccttatctg tagaccaga cctgaccact 494
Arg

taagttccag attcattttt ctttccgacg tcacaaattt cttagggagg tggggggggg 554

ggagaaccat ttcctcagct gggacctcag cctgcaccgc ctgcctccat ggagctgagc 614

ccagccaccc ctgccttggt gcatggggcc cagccgggtg gccctcctcc gtctgcactt 674

catcaacgct gagggaaagc actgcatccc atgactgtcc cctcctcaga gcaaagtgca 734

gcattacagt ggaggcagat atgtgtggga ggggggtctt ctgtacctgg gagtggcaca 794

gacatgtttc ttcttagcct tatttattat tgtgtggtat ttaaacaagt gtctttgttt 854

gtgctgggga caggagtggt cttggagctg ggggccagct gactcgggtt tagagagtcc 914

ctgggaataa gcactgtgtg taaaattctg ctacctcact gggatcctgg ggccgacaca 974

ggggacagga gaaaggggtca gagatgctgc tcttgtctgc cactcagcag ctggccctca 1034

gccaagcagt aatttattgt ttttccttgt atttaaagtt aagaaataaa atatgttatc 1094

aaagagttaa taatatatag aagagtagcc taaaaggctg catttggtgt gtgtggccag 1154

gccggggcgg gtggggggga ggggtgtgtc actgaatgtg ctctttcact gactttgtca 1214

aactggaagc cagaaataaa gatggtgaca agagaaaaaa aaaaaaaaaa aaaaaaaaaa 1274

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1302

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<210> 92  
 <211> 131  
 <212> PRT

<213> Canis familiaris

<400> 92

Met Ala Leu Trp Leu Thr Val Val Ile Ala Leu Thr Cys Leu Gly Gly  
1 5 10 15

Leu Ala Ser Pro Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu  
20 25 30

Ile Glu Glu Leu Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn  
35 40 45

Gly Ser Met Val Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala  
50 55 60

Ala Leu Glu Ser Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg  
65 70 75 80

Thr Gln Arg Met Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly  
85 90 95

Gln Ile Ser Ser Glu Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln  
100 105 110

Leu Val Lys Asn Leu Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly  
115 120 125

Asn Phe Arg  
130

<210> 93

<211> 1302

<212> DNA

<213> Canis familiaris

<400> 93

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tcaccatctt tatttctggc ttccagtttg acaaagtcag tgaaagagca cattcagtga 120

caacaccctc cccccaccc gccccggcct ggccacacac accaaatgca gccttttagg 180

ctactcttct atatattatt aactctttga taacatattt tatttcttaa ctttaaatac 240

aaggaaaaac aataaattac tgcttggctg agggccagct gctgagtggc agacaagagc 300

agcatctctg accctttctc ctgtcccctg tgtcggcccc aggatcccag tgaggtagca 360

gaattttaca cacagtgtt attcccaggg actctctaaa cccgagtcac tgggccccca 420  
 gctccaagcc actccctgtc cccagcacia acaaagacac ttgttttaat aacacacaat 480  
 aataaataag gctaagaaga aacatgtctg tgccactccc aggtacagca agaccccctc 540  
 ccacacatat ctgcctccac tgtaatgtct cactttgtct tgaggagggg acagtcattg 600  
 gatgcagtgc tttccctcag cgttgatgaa gtgcagacgg aggagggcca cccggctggg 660  
 ccccatgcac caaggcaggg gtggctgggc tcagctccat ggaggcaggc ggtgcaggct 720  
 gaggtcccag ctgaggaaat ggttctcccc cccccacc tccctaagaa atttgtgacg 780  
 tcggaaagaa aaatgaatct ggaacttaag tggtcaggct tgggtctaca gataaggatg 840  
 ctaagttttc atgcttcatc tgaaatttcc atggcgataa actcccctta cataggtagg 900  
 caggtttttc accaactgga tcacttcaat tttgggtgtct cggctgcgtt cactggaaat 960  
 ctgccctgcc gcgggctttt gagagcacag tgctttcagc atcctctggg tcctttggat 1020  
 ggcgctgcag tcggagacat tgatcagaga ttctagagct gcgcagtaca tgccggcggg 1080  
 caggttgacg ctccacacca tgctgccgtt gcagagggat gcctgattct gggatgatgtt 1140  
 gaccagctcc tcaatgagct ccttgagggt tggggaggga gtcacagggc tcggggaggc 1200  
 aaggccaccg aggcaggtga gagcaatgac cacagtcaac cagagcgcca tggagcccag 1260  
 agccaatgca ggaggagcga gggaagagca ggcaggctcg ag 1302

<210> 94

<211> 393

<212> DNA

<213> *Canis familiaris*

<400> 94

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 agccctgtga ctccctcccc aaccctcaag gagctcattg aggagctggg caacatcacc 120  
 cagaatcagg catccctctg caacggcagc atgggtgtgga gcgtcaacct gaccgccggc 180  
 atgtactgcg cagctctaga atctctgac aatgtctccg actgcagcgc catccaaagg 240



acccagagga tgctgaaagc actgtgctct caaaagcccc cggcagggca gatttccagt 300  
 gaacgcagcc gagacaccaa aattgaagtg atccagttgg tgaaaaacct gctcacctat 360  
 gtaaggggag tttatcgcca tggaaatttc aga 393

<210> 95  
 <211> 393  
 <212> DNA  
 <213> Canis familiaris

<400> 95  
 tctgaaattt ccatggcgat aaactcccct tacataggtg agcagggtttt tcaccaactg 60  
 gatcacttca attttgggtgt ctcggtgctg ttcactggaa atctgccctg ccgcgggctt 120  
 ttgagagcac agtgctttca gcatcctctg ggtccttttg atggcgctgc agtcggagac 180  
 attgatcaga gattctagag ctgcgcagta catgccggcg gtcagggttg cgctccacac 240  
 catgctgccg ttgcagaggg atgcctgatt ctgggtgatg ttgaccagct cctcaatgag 300  
 ctccttgagg gttggggagg gaggcacagg gctcggggag gcaaggccac cgaggcaggt 360  
 gagagcaatg accacagtca accagagcgc cat 393

<210> 96  
 <211> 333  
 <212> DNA  
 <213> Canis familiaris

<220>  
 <221> CDS  
 <222> (1)..(333)

<400> 96  
 agc cct gtg act ccc tcc cca acc ctc aag gag ctc att gag gag ctg 48  
 Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu Ile Glu Glu Leu  
 1 5 10 15  
 gtc aac atc acc cag aat cag gca tcc ctc tgc aac ggc agc atg gtg 96  
 Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn Gly Ser Met Val  
 20 25 30  
 tgg agc gtc aac ctg acc gcc ggc atg tac tgc gca gct cta gaa tct 144  
 Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala Leu Glu Ser

35	40	45	
ctg atc aat gtc tcc gac tgc agc gcc atc caa agg acc cag agg atg	192		
Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg Thr Gln Arg Met			
50	55	60	
ctg aaa gca ctg tgc tct caa aag ccc gcg gca ggg cag att tcc agt	240		
Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly Gln Ile Ser Ser			
65	70	75	80
gaa cgc agc cga gac acc aaa att gaa gtg atc cag ttg gtg aaa aac	288		
Glu Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln Leu Val Lys Asn			
85	90	95	
ctg ctc acc tat gta agg gga gtt tat cgc cat gga aat ttc aga	333		
Leu Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly Asn Phe Arg			
100	105	110	

<210> 97  
 <211> 111  
 <212> PRT  
 <213> Canis familiaris

<400> 97  
 Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu Ile Glu Glu Leu  
 1 5 10 15  
 Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn Gly Ser Met Val  
 20 25 30  
 Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala Leu Glu Ser  
 35 40 45  
 Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg Thr Gln Arg Met  
 50 55 60  
 Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly Gln Ile Ser Ser  
 65 70 75 80  
 Glu Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln Leu Val Lys Asn  
 85 90 95  
 Leu Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly Asn Phe Arg  
 100 105 110

<210> 98

<211> 333  
 <212> DNA  
 <213> Canis familiaris

<400> 98  
 tctgaaattt ccatggcgat aaactcccct tacataggtg agcaggtttt tcaccaactg 60  
 gatcacttca attttgggtgt ctgggctgcg ttacttgga atctgccctg ccgcgggctt 120  
 ttgagagcac agtgctttca gcacacctctg ggtccttttg atggcgctgc agtcggagac 180  
 attgatcaga gattctagag ctgcgcagta catgccggcg gtcagggttga cgctccacac 240  
 catgctgccg ttgcagaggg atgcctgatt ctgggtgatg ttgaccagct cctcaatgag 300  
 ctccttgagg gttggggagg gagtcacagg gct 333

<210> 99  
 <211> 1269  
 <212> DNA  
 <213> Canis familiaris

<220>  
 <221> CDS  
 <222> (57)..(446)

<400> 99  
 ccagcctacg acctgcctgc tcttccctcg ctccctcctgc attggctctg ggctcc atg 59  
 Met  
 1  
 gcg ctc tgg ttg act gtg gtc att gct ctc acc tgc ctc ggt ggc ctt 107  
 Ala Leu Trp Leu Thr Val Val Ile Ala Leu Thr Cys Leu Gly Gly Leu  
 5 10 15  
 gcc tcc ccg agc cct gtg act ccc tcc cca acc ctc aag gag ctc att 155  
 Ala Ser Pro Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu Ile  
 20 25 30  
 gag gag ctg gtc aac atc acc cag aat cag gca tcc ctc tgc aac ggc 203  
 Glu Glu Leu Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn Gly  
 35 40 45  
 agc atg gtg tgg agc gtc aac ctg acc gcc ggc atg tac tgc gca gct 251  
 Ser Met Val Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala  
 50 55 60 65

cta gaa tct ctg atc aat gtc tcc gac tgc agc gcc atc caa agg acc 299  
 Leu Glu Ser Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg Thr  
                     70                    75                    80

cag agg atg ctg aaa gca ctg tgc tct caa aag ccc gcg gca ggg att 347  
 Gln Arg Met Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly Ile  
                     85                    90                    95

tcc agt gaa cgc agc cga gac acc aaa att gaa gtg atc cag ttg gtg 395  
 Ser Ser Glu Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln Leu Val  
                     100                    105                    110

aaa aac ctg ctc acc tat gta agg gga gtt tat cgc cat gga aat ttc 443  
 Lys Asn Leu Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly Asn Phe  
                     115                    120                    125

aga tgaagcatga aaacttagca tccttatctg tagaccacaga cctgaccact 496  
 Arg  
 130

taagttccag attcattttt ctttccgacg tcacaaattt cttagggagg tggggggggg 556  
 ggagaaccat ttcctcagct gggacctcag cctgcaccgc ctgcctccat ggagctgagc 616  
 ccagccaccc ctgccttggt gcatggggcc cagccgggtg gccctcctcc gtctgcactt 676  
 catcaacgct gagggaaagc actgcatccc atgactgtcc cctcctcaga gcaaagtgca 736  
 gcattacagt ggaggcagat atgtgtggga gggggtcttg ctgtacctgg gagtggcaca 796  
 gacatgtttc ttcttagcct tatttattat tgtgtgttat ttaaacaagt gtctttgttt 856  
 gtgctgggga caggagtggt cttggagctg ggggccagtg gactcgggtt tagagagtcc 916  
 ctgggaataa gcactgtgtg taaaattctg ctacctcact gggatcctgg ggccgacaca 976  
 ggggacagga gaaaggggtca gagatgctgc tcttgtctgc cactcagcag ctggccctca 1036  
 gccaaagcagt aatttattgt ttttccttgt atttaaagtt aagaaataaa atatgttatc 1096  
 aaagagttaa taatatatag aagagtagcc taaaaggctg catttggtgt gtgtggccag 1156  
 gccggggcgg gtggggggga ggggtgtgtc actgaatgtg ctctttcact gactttgtca 1216  
 aactggaagc cagaaataaa gatggtgaca agagaaaaaa aaaaaaaaaa aaa 1269

<210> 100

<211> 130  
 <212> PRT  
 <213> Canis familiaris

<400> 100  
 Met Ala Leu Trp Leu Thr Val Val Ile Ala Leu Thr Cys Leu Gly Gly  
   1                  5                  10                  15  
 Leu Ala Ser Pro Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu  
                   20                  25                  30  
 Ile Glu Glu Leu Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn  
           35                  40                  45  
 Gly Ser Met Val Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala  
           50                  55                  60  
 Ala Leu Glu Ser Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg  
   65                  70                  75                  80  
 Thr Gln Arg Met Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly  
                   85                  90                  95  
 Ile Ser Ser Glu Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln Leu  
                   100                  105                  110  
 Val Lys Asn Leu Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly Asn  
           115                  120                  125  
 Phe Arg  
   130

<210> 101  
 <211> 1269  
 <212> DNA  
 <213> Canis familiaris

<400> 101  
 tttttttttt tttttttttt tcttggtcacc atctttatct ctggcttcca gtttgacaaa 60  
 gtcagtgaaa gagcacattc agtgacaaca ccctcccccc caccgcgccg ggctgggcca 120  
 cacacaccaa atgcagcctt ttaggctact ctcttatata ttattaactc tttgataaca 180  
 tatctttatct cttaacttta aatacaagga aaaacaataa attactgctt ggctgagggc 240  
 cagctgctga gtggcagaca agagcagcat ctctgaccct ttctcctgtc ccctgtgtcg 300

gccccaggat cccagtgagg tagcagaatt ttacacacag tgcttattcc cagggactct 360  
 ctaaaccgga gtcactgggc cccagctcc aagccactcc ctgtccccag cacaaacaaa 420  
 gacacttggt taaataacac acaataataa ataaggctaa gaagaaacat gtctgtgcca 480  
 ctcccaggta cagcaagacc ccctcccaca catatctgcc tccactgtaa tgctgcactt 540  
 tgctctgagg aggggacagt catgggatgc agtgctttcc ctcagcgttg atgaagtgca 600  
 gacggaggag ggccacccgg ctgggccccca tgcaccaagg caggggtggc tgggctcagc 660  
 tccatggagg caggcgggtgc aggctgaggt cccagctgag gaaatgggtc tccccccccc 720  
 ccacctccct aagaaatttg tgacgtcgga aagaaaaatg aatctggaac ttaagtggtc 780  
 aggtctgggt ctacagataa ggatgctaag ttttcatgct tcatctgaaa tttccatggc 840  
 gataaactcc ccttacatag gtgagcaggt ttttcaccaa ctggatcact tcaatttttg 900  
 tgtctcggct gcgttcactg gaaatccctg ccgcgggctt ttgagagcac agtgctttca 960  
 gcatcctctg ggtccttttg atggcgctgc agtcggagac attgatcaga gattctagag 1020  
 ctgcgcagta catgccggcg gtcaggttga cgctccacac catgctgccg ttgcagaggg 1080  
 atgcctgatt ctgggtgatg ttgaccagct cctcaatgag ctccctgagg gttggggagg 1140  
 gagtcacagg gctcggggag gcaaggccac cgaggcaggt gagagcaatg accacagtca 1200  
 accagagcgc catggagccc agagccaatg caggaggagc gaggggaagag caggcaggtc 1260  
 gtaggctgg 1269

<210> 102  
 <211> 390  
 <212> DNA  
 <213> Canis familiaris

<400> 102  
 atggcgctct ggttgactgt ggtcattgct ctacactgcc tcggtggcct tgccctcccc 60  
 agccctgtga ctccctcccc aaccctcaag gagctcattg aggagctggc caacatcacc 120  
 cagaatcagg catccctctg caacggcagc atggtgtgga gcgtcaacct gaccgccggc 180

atgtactgcg cagctctaga atctctgac aatgtctccg actgcagcgc catccaaagg 240  
 acccagagga tgctgaaagc actgtgctct caaaagcccg cggcagggat ttccagtga 300  
 cgcagccgag acaccaaaat tgaagtgatc cagttgggtga aaaacctgct cacctatgta 360  
 aggggagttt atcgccatgg aaatttcaga 390

<210> 103  
 <211> 390  
 <212> DNA  
 <213> Canis familiaris

<400> 103  
 tctgaaattt ccatggcgat aaactcccct tacataggtg agcaggtttt tcaccaactg 60  
 gatcacttca attttgggtgt ctcggctgcg ttcactggaa atccctgccg cgggcttttg 120  
 agagcacagt gctttcagca tcctctgggt cctttggatg gcgctgcagt cggagacatt 180  
 gatcagagat tctagagctg cgcagtacat gccggcggtc aggttgacgc tccacaccat 240  
 gctgccgttg cagaggggatg cctgattctg ggtgatgttg accagctcct caatgagctc 300  
 cttgaggggtt ggggagggag tcacagggct cggggaggga aggccaccga ggcagggtgag 360  
 agcaatgacc acagtcaacc agagcgccat 390

<210> 104  
 <211> 330  
 <212> DNA  
 <213> Canis familiaris

<220>  
 <221> CDS  
 <222> (1)..(330)

<400> 104  
 agc cct gtg act ccc tcc cca acc ctc aag gag ctc att gag gag ctg 48  
 Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu Ile Glu Glu Leu  
 1 5 10 15  
 gtc aac atc acc cag aat cag gca tcc ctc tgc aac ggc agc atg gtg 96  
 Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn Gly Ser Met Val  
 20 25 30

tgg agc gtc aac ctg acc gcc ggc atg tac tgc gca gct cta gaa tct	144
Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala Leu Glu Ser	
35 40 45	

ctg atc aat gtc tcc gac tgc agc gcc atc caa agg acc cag agg atg	192
Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg Thr Gln Arg Met	
50 55 60	

ctg aaa gca ctg tgc tct caa aag ccc gcg gca ggg att tcc agt gaa	240
Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly Ile Ser Ser Glu	
65 70 75 80	

cgc agc cga gac acc aaa att gaa gtg atc cag ttg gtg aaa aac ctg	288
Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln Leu Val Lys Asn Leu	
85 90 95	

ctc acc tat gta agg gga gtt tat cgc cat gga aat ttc aga	330
Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly Asn Phe Arg	
100 105 110	

<210> 105  
 <211> 110  
 <212> PRT  
 <213> Canis familiaris

<400> 105
Ser Pro Val Thr Pro Ser Pro Thr Leu Lys Glu Leu Ile Glu Glu Leu
1 5 10 15

Val Asn Ile Thr Gln Asn Gln Ala Ser Leu Cys Asn Gly Ser Met Val
20 25 30

Trp Ser Val Asn Leu Thr Ala Gly Met Tyr Cys Ala Ala Leu Glu Ser
35 40 45

Leu Ile Asn Val Ser Asp Cys Ser Ala Ile Gln Arg Thr Gln Arg Met
50 55 60

Leu Lys Ala Leu Cys Ser Gln Lys Pro Ala Ala Gly Ile Ser Ser Glu
65 70 75 80

Arg Ser Arg Asp Thr Lys Ile Glu Val Ile Gln Leu Val Lys Asn Leu
85 90 95

Leu Thr Tyr Val Arg Gly Val Tyr Arg His Gly Asn Phe Arg
100 105 110



<210> 106  
 <211> 330  
 <212> DNA  
 <213> Canis familiaris

<400> 106  
 tctgaaattt ccatggcgat aaactcccct tacataggtg agcaggtttt tcaccaactg 60  
 gatcacttca attttgggtgt ctcggctgcg ttcactggaa atccctgccg cgggcttttg 120  
 agagcacagt gctttcagca tcctctgggt cctttggatg gcgctgcagt cggagacatt 180  
 gatcagagat tctagagctg cgcagtacat gccggcggtc aggttgacgc tccacaccat 240  
 gctgccgttg cagaggggatg cctgattctg ggtgatgttg accagctcct caatgagctc 300  
 cttgagggtt ggggagggag tcacagggt 330

<210> 107  
 <211> 567  
 <212> DNA  
 <213> Felis catus

<220>  
 <221> CDS  
 <222> (1)..(567)

<400> 107  
 atg gcg ctg ccc tct tcc ttc ttg gtg gcc ctg gtg gcg ctg ggc tgc 48  
 Met Ala Leu Pro Ser Ser Phe Leu Val Ala Leu Val Ala Leu Gly Cys  
 1 5 10 15  
 aac tcc gtc tgc tct ctg ggc tgt gac ctg cct cag acc cac ggc ctg 96  
 Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu  
 20 25 30  
 ctg aac agg agg gcc ttg acg ctc ctg gga caa atg agg aga ctc cct 144  
 Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro  
 35 40 45  
 gcc agc tcc tgt cag aag gac aga aat gac ttc gcc ttc ccc cag gac 192  
 Ala Ser Ser Cys Gln Lys Asp Arg Asn Asp Phe Ala Phe Pro Gln Asp  
 50 55 60  
 gtg ttt ggt gga gac cag tcc cac aag gcc caa gcc ctc tcg gtg gtg 240  
 Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val

65	70	75	80	
cac gtg acg aac cag aag atc ttc cac ttc ttc tgc aca gag gcg tcc				288
His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser				
	85	90	95	
tcg tct gct gct tgg aac acc acc ctc ctg gag gaa ttc tgc acg gga				336
Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly				
	100	105	110	
ctt gat tgg cag ctg acc cgc ctg gaa gcc tgt gtc atg cag gag gtg				384
Leu Asp Trp Gln Leu Thr Arg Leu Glu Ala Cys Val Met Gln Glu Val				
	115	120	125	
ggg gag gga gag gct ccc ctc acg aac gag gac tcc atc ctg agg aac				432
Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ser Ile Leu Arg Asn				
	130	135	140	
tac ttc caa aga ctc tcc ctc tac ctg caa gag aag aaa tac agc cct				480
Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro				
	145	150	155	160
tgt gcc tgg gag atc gtc aga gca gaa atc atg aga tcc ttg tat tat				528
Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr				
	165	170	175	
tca tca aca gcc ttg cag aaa aga tta agg agc gag aaa				567
Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys				
	180	185		

<210> 108  
 <211> 189  
 <212> PRT  
 <213> Felis catus

<400> 108  
 Met Ala Leu Pro Ser Ser Phe Leu Val Ala Leu Val Ala Leu Gly Cys  
 1 5 10 15  
 Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu  
 20 25 30  
 Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro  
 35 40 45  
 Ala Ser Ser Cys Gln Lys Asp Arg Asn Asp Phe Ala Phe Pro Gln Asp  
 50 55 60

Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val  
 65 70 75 80

His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser  
 85 90 95

Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly  
 100 105 110

Leu Asp Trp Gln Leu Thr Arg Leu Glu Ala Cys Val Met Gln Glu Val  
 115 120 125

Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ser Ile Leu Arg Asn  
 130 135 140

Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro  
 145 150 155 160

Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr  
 165 170 175

Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys  
 180 185

<210> 109  
 <211> 567  
 <212> DNA  
 <213> Felis catus

<400> 109  
 tttctcgctc cttaatcttt tctgcaaggc tgttgatgaa taatacaagg atctcatgat 60  
 ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagaggga 120  
 gagtcttttg aagtagttcc tcaggatgga gtcctcgttc gtgaggggag cctctccctc 180  
 cccacctcc tgcattgacac aggcctccag gcgggtcagc tgccaatcaa gtcccgtgca 240  
 gaattcctcc aggaggggtgg tgttccaagc agcagacgag gacgcctctg tgcagaagaa 300  
 gtggaagatc ttctgggttcg tcacgtgcac caccgagagg gcttgggcct tgtgggactg 360  
 gtctccacca aacacgtcct gggggaaggc gaagtcattt ctgtccttct gacaggagct 420  
 ggcagggagt ctctcattt gtcccaggag cgtcaaggcc ctctgttca gcaggccgtg 480

ggctctgaggc aggtcacagc ccagagagca gacggagttg cagcccagcg ccaccagggc 540

caccaagaag gaagagggca gcgccat 567

<210> 110  
<211> 567  
<212> DNA  
<213> Felis catus

<220>  
<221> CDS  
<222> (1)..(567)

<400> 110  
atg gcg ctg ccc tct tcc ttc ttg gtg gcc ctg gtg gcg ctg ggc tgc 48  
Met Ala Leu Pro Ser Ser Phe Leu Val Ala Leu Val Ala Leu Gly Cys  
1 5 10 15  
  
aac tcc gtc tgc tct ctg ggc tgt gac ctg cct cag acc cac ggc ctg 96  
Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu  
20 25 30  
  
ctg aac agg agg gcc ttg acg ctc ctg gga caa atg agg aga ctc cct 144  
Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro  
35 40 45  
  
gcc agc tcc tgt cag aag gac agg aat gac ttc gcc ttc ccc cag gac 192  
Ala Ser Ser Cys Gln Lys Asp Arg Asn Asp Phe Ala Phe Pro Gln Asp  
50 55 60  
  
gtg ttc ggt gga gac cag tcc cac aag gct caa gcc ctc tcg gtg gtg 240  
Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val  
65 70 75 80  
  
cac gtg acg aac cag gag atc ttc cac ttc ttc tgc aca gag gcg tcc 288  
His Val Thr Asn Gln Glu Ile Phe His Phe Phe Cys Thr Glu Ala Ser  
85 90 95  
  
tcg tct gct gct tgg aac acc acc ctc ctg gag gaa ttc tgc acg gga 336  
Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly  
100 105 110  
  
ctt gat cgg cag ctg acc cgc ctg gaa gcc tgt gtc gtg cag gag gtg 384  
Leu Asp Arg Gln Leu Thr Arg Leu Glu Ala Cys Val Val Gln Glu Val  
115 120 125  
  
ggg gag gga gag gct ccc ctc acg aac gag gac tcc ctc ctg agg aac 432

Gly	Glu	Gly	Glu	Ala	Pro	Leu	Thr	Asn	Glu	Asp	Ser	Leu	Leu	Arg	Asn	
130						135					140					
tac	ttc	caa	aga	ctc	tcc	ctc	tac	ctg	caa	gag	aag	aaa	tac	agc	cct	480
Tyr	Phe	Gln	Arg	Leu	Ser	Leu	Tyr	Leu	Gln	Glu	Lys	Lys	Tyr	Ser	Pro	
145					150					155					160	
tgt	gcc	tgg	gag	atc	gtc	aga	gca	gaa	atc	atg	aga	tcc	ttg	tat	tat	528
Cys	Ala	Trp	Glu	Ile	Val	Arg	Ala	Glu	Ile	Met	Arg	Ser	Leu	Tyr	Tyr	
			165					170						175		
tca	tca	aca	gcc	ttg	caa	aaa	aga	tta	agg	agc	gag	aaa				567
Ser	Ser	Thr	Ala	Leu	Gln	Lys	Arg	Leu	Arg	Ser	Glu	Lys				
			180					185								

<210> 111  
 <211> 189  
 <212> PRT  
 <213> Felis catus

<400> 111

Met	Ala	Leu	Pro	Ser	Ser	Phe	Leu	Val	Ala	Leu	Val	Ala	Leu	Gly	Cys	
1				5					10					15		
Asn	Ser	Val	Cys	Ser	Leu	Gly	Cys	Asp	Leu	Pro	Gln	Thr	His	Gly	Leu	
			20					25					30			
Leu	Asn	Arg	Arg	Ala	Leu	Thr	Leu	Leu	Gly	Gln	Met	Arg	Arg	Leu	Pro	
		35					40					45				
Ala	Ser	Ser	Cys	Gln	Lys	Asp	Arg	Asn	Asp	Phe	Ala	Phe	Pro	Gln	Asp	
	50					55					60					
Val	Phe	Gly	Gly	Asp	Gln	Ser	His	Lys	Ala	Gln	Ala	Leu	Ser	Val	Val	
65					70					75					80	
His	Val	Thr	Asn	Gln	Glu	Ile	Phe	His	Phe	Phe	Cys	Thr	Glu	Ala	Ser	
				85					90					95		
Ser	Ser	Ala	Ala	Trp	Asn	Thr	Thr	Leu	Leu	Glu	Glu	Phe	Cys	Thr	Gly	
		100						105					110			
Leu	Asp	Arg	Gln	Leu	Thr	Arg	Leu	Glu	Ala	Cys	Val	Val	Gln	Glu	Val	
	115					120						125				
Gly	Glu	Gly	Glu	Ala	Pro	Leu	Thr	Asn	Glu	Asp	Ser	Leu	Leu	Arg	Asn	
130						135					140					

Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro  
 145 150 155 160

Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr  
 165 170 175

Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys  
 180 185

<210> 112  
 <211> 567  
 <212> DNA  
 <213> Felis catus

<400> 112  
 tttctcgctc cttaatcttt ttgcaaggc tgttgatgaa taatacaagg atctcatgat 60  
 ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagaggga 120  
 gagtctttgg aagtagttcc tcaggaggga gtcctcgttc gtgaggggag cctctccctc 180  
 cccacctcc tgcacgacac aggcttccag gcgggtcagc tgccgatcaa gtcccgtgca 240  
 gaattcctcc aggaggggtg tgttccaagc agcagacgag gacgcctctg tgcagaagaa 300  
 gtggaagatc tcctggttcg tcacgtgcac caccgagagg gcttgagcct tgtgggactg 360  
 gtctccaccg aacacgtcct gggggaaggc gaagtcattc ctgtccttct gacaggagct 420  
 ggcagggagt ctctcathtt gtcccaggag cgtcaaggcc ctctgttca gcaggccgtg 480  
 ggtctgaggc aggtcacagc ccagagagca gacggagttg cagcccagcg ccaccagggc 540  
 caccaagaag gaagagggca gcgccat 567

<210> 113  
 <211> 498  
 <212> DNA  
 <213> Felis catus

<220>  
 <221> CDS  
 <222> (1)..(498)

<400> 113

tgt gac ctg cct cag acc cac ggc ctg ctg aac agg agg gcc ttg acg	48
Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr	
1 5 10 15	
ctc ctg gga caa atg agg aga ctc cct gcc agc tcc tgt cag aag gac	96
Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp	
20 25 30	
aga aat gac ttc gcc ttc ccc cag gac gtg ttt ggt gga gac cag tcc	144
Arg Asn Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser	
35 40 45	
cac aag gcc caa gcc ctc tcg gtg gtg cac gtg acg aac cag aag atc	192
His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile	
50 55 60	
ttc cac ttc ttc tgc aca gag gcg tcc tcg tct gct gct tgg aac acc	240
Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr	
65 70 75 80	
acc ctc ctg gag gaa ttc tgc acg gga ctt gat tgg cag ctg acc cgc	288
Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Trp Gln Leu Thr Arg	
85 90 95	
ctg gaa gcc tgt gtc atg cag gag gtg ggg gag gga gag gct ccc ctc	336
Leu Glu Ala Cys Val Met Gln Glu Val Gly Glu Gly Glu Ala Pro Leu	
100 105 110	
acg aac gag gac tcc atc ctg agg aac tac ttc caa aga ctc tcc ctc	384
Thr Asn Glu Asp Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu	
115 120 125	
tac ctg caa gag aag aaa tac agc cct tgt gcc tgg gag atc gtc aga	432
Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg	
130 135 140	
gca gaa atc atg aga tcc ttg tat tat tca tca aca gcc ttg cag aaa	480
Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys	
145 150 155 160	
aga tta agg agc gag aaa	498
Arg Leu Arg Ser Glu Lys	
165	

<210> 114  
 <211> 166  
 <212> PRT

<213> Felis catus

<400> 114

Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr  
1 5 10 15

Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp  
20 25 30

Arg Asn Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser  
35 40 45

His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile  
50 55 60

Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr  
65 70 75 80

Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Trp Gln Leu Thr Arg  
85 90 95

Leu Glu Ala Cys Val Met Gln Glu Val Gly Glu Gly Glu Ala Pro Leu  
100 105 110

Thr Asn Glu Asp Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu  
115 120 125

Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg  
130 135 140

Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys  
145 150 155 160

Arg Leu Arg Ser Glu Lys  
165

<210> 115

<211> 498

<212> DNA

<213> Felis catus

<400> 115

tttctcgctc cttaatcttt tctgcaaggc tgttgatgaa taatacaagg atctcatgat 60

ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagaggga 120

gagtctttgg aagtagttcc tcaggatgga gtcctcgttc gtgaggggag cctctccctc 180



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ccccacctcc tgcacgacac aggcctccag gcgggtcagc tgccaatcaa gtcccgtgca 240
gaattcctcc aggaggggtgg tgttccaagc agcagacgag gacgcctctg tgcagaagaa 300
gtggaagatc ttctgggttcg tcacgtgcac caccgagagg gcttgggcct tgtgggactg 360
gtctccacca aacacgtcct gggggaaggc gaagtcattt ctgtccttct gacaggagct 420
ggcagggagt ctcctcattt gtcccaggag cgtcaaggcc ctcctgttca gcaggccgtg 480
ggtctgaggc aggtcaca

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<210> 116
<211> 498
<212> DNA
<213> Felis catus

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<220>
<221> CDS
<222> (1)..(498)

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<400> 116
tgt gac ctg cct cag acc cac ggc ctg ctg aac agg agg gcc ttg acg 48
Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr
1 5 10 15

ctc ctg gga caa atg agg aga ctc cct gcc agc tcc tgt cag aag gac 96
Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp
20 25 30

agg aat gac ttc gcc ttc ccc cag gac gtg ttc ggt gga gac cag tcc 144
Arg Asn Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser
35 40 45

cac aag gct caa gcc ctc tcg gtg gtg cac gtg acg aac cag gag atc 192
His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Glu Ile
50 55 60

ttc cac ttc ttc tgc aca gag gcg tcc tcg tct gct gct tgg aac acc 240
Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr
65 70 75 80

acc ctc ctg gag gaa ttc tgc acg gga ctt gat cgg cag ctg acc cgc 288
Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Arg Gln Leu Thr Arg
85 90 95

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ctg gaa gcc tgt gtc gtg cag gag gtg ggg gag gga gag gct ccc ctc 336  
 Leu Glu Ala Cys Val Val Gln Glu Val Gly Glu Gly Glu Ala Pro Leu  
                   100                                  105                                  110

acg aac gag gac tcc ctc ctg agg aac tac ttc caa aga ctc tcc ctc 384  
 Thr Asn Glu Asp Ser Leu Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu  
                   115                                  120                                  125

tac ctg caa gag aag aaa tac agc cct tgt gcc tgg gag atc gtc aga 432  
 Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg  
                   130                                  135                                  140

gca gaa atc atg aga tcc ttg tat tat tca tca aca gcc ttg caa aaa 480  
 Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys  
 145                                  150                                  155                                  160

aga tta agg agc gag aaa 498  
 Arg Leu Arg Ser Glu Lys  
                                   165

<210> 117  
 <211> 166  
 <212> PRT  
 <213> Felis catus

<400> 117  
 Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr  
   1                                  5                                  10                                  15  
 Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp  
                   20                                  25                                  30  
 Arg Asn Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser  
                   35                                  40                                  45  
 His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Glu Ile  
                   50                                  55                                  60  
 Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr  
   65                                  70                                  75                                  80  
 Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Arg Gln Leu Thr Arg  
                   85                                  90                                  95  
 Leu Glu Ala Cys Val Val Gln Glu Val Gly Glu Gly Glu Ala Pro Leu  
                   100                                  105                                  110

Thr Asn Glu Asp Ser Leu Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu  
 115 120 125

Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg  
 130 135 140

Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys  
 145 150 155 160

Arg Leu Arg Ser Glu Lys  
 165

<210> 118  
 <211> 498  
 <212> DNA  
 <213> Felis catus

<400> 118  
 tttctcgctc cttaatcttt tttgcaaggc tgttgatgaa taatacaagg atctcatgat 60  
 ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagaggga 120  
 gagtcttttg aagtagttcc tcaggaggga gtccctcggtc gtgaggggag cctctccctc 180  
 cccacacctc tgcacgacac aggcctccag gcgggtcagc tgccgatcaa gtcccgtgca 240  
 gaattcctcc aggaggggtgg tgttccaagc agcagacgag gacgcctctg tgcagaagaa 300  
 gtggaagatc tcctgggttcg tcacgtgcac caccgagagg gcttgagcct tgtgggactg 360  
 gtctccaccg aacacgtcct gggggaaggc gaagtcattc ctgtccttct gacaggagct 420  
 ggcagggagt ctctcathtt gtcccaggag cgtcaaggcc ctctgttca gcaggccgtg 480  
 ggtctgaggc aggtcaca 498

<210> 119  
 <211> 444  
 <212> DNA  
 <213> Felis catus

<220>  
 <221> CDS  
 <222> (10)..(441)

<400> 119

ggatccacc atg tgg ctg cag aac ctg ctt ttc ctg ggc act gtg gtc tgc 51  
 Met Trp Leu Gln Asn Leu Leu Phe Leu Gly Thr Val Val Cys  
 1 5 10

agc atc tct gca ccc acc agt tca ccc agc tct gtc act cgg ccc tgg 99  
 Ser Ile Ser Ala Pro Thr Ser Ser Pro Ser Ser Val Thr Arg Pro Trp  
 15 20 25 30

caa cac gtg gat gcc atc aag gag gcc ctg agc ctt ctg aac aac agt 147  
 Gln His Val Asp Ala Ile Lys Glu Ala Leu Ser Leu Leu Asn Asn Ser  
 35 40 45

agt gaa ata act gct gtg atg aat gaa gca gta gaa gtc gtc tct gaa 195  
 Ser Glu Ile Thr Ala Val Met Asn Glu Ala Val Glu Val Val Ser Glu  
 50 55 60

atg ttt gac cct gag gag ccg aaa tgc ctg cag act cac cta aag ctg 243  
 Met Phe Asp Pro Glu Glu Pro Lys Cys Leu Gln Thr His Leu Lys Leu  
 65 70 75

tac gag cag ggc cta cgg ggc agc ctc atc agc ctc aag gag cct ctg 291  
 Tyr Glu Gln Gly Leu Arg Gly Ser Leu Ile Ser Leu Lys Glu Pro Leu  
 80 85 90

aga atg atg gcc aac cat tac aag cag cac tgc ccc ctt act ccg gaa 339  
 Arg Met Met Ala Asn His Tyr Lys Gln His Cys Pro Leu Thr Pro Glu  
 95 100 105 110

acg ccc tgt gaa acc cag act atc acc ttc aaa aat ttc aaa gag aat 387  
 Thr Pro Cys Glu Thr Gln Thr Ile Thr Phe Lys Asn Phe Lys Glu Asn  
 115 120 125

ctg aag gat ttt ctg ttt aac aac ccc ttt gac tgc tgg gga cca gac 435  
 Leu Lys Asp Phe Leu Phe Asn Asn Pro Phe Asp Cys Trp Gly Pro Asp  
 130 135 140

cag aag taa 444  
 Gln Lys

<210> 120  
 <211> 144  
 <212> PRT  
 <213> Felis catus

<400> 120  
 Met Trp Leu Gln Asn Leu Leu Phe Leu Gly Thr Val Val Cys Ser Ile  
 1 5 10 15

Ser Ala Pro Thr Ser Ser Pro Ser Ser Val Thr Arg Pro Trp Gln His  
 20 25 30

Val Asp Ala Ile Lys Glu Ala Leu Ser Leu Leu Asn Asn Ser Ser Glu  
 35 40 45

Ile Thr Ala Val Met Asn Glu Ala Val Glu Val Val Ser Glu Met Phe  
 50 55 60

Asp Pro Glu Glu Pro Lys Cys Leu Gln Thr His Leu Lys Leu Tyr Glu  
 65 70 75 80

Gln Gly Leu Arg Gly Ser Leu Ile Ser Leu Lys Glu Pro Leu Arg Met  
 85 90 95

Met Ala Asn His Tyr Lys Gln His Cys Pro Leu Thr Pro Glu Thr Pro  
 100 105 110

Cys Glu Thr Gln Thr Ile Thr Phe Lys Asn Phe Lys Glu Asn Leu Lys  
 115 120 125

Asp Phe Leu Phe Asn Asn Pro Phe Asp Cys Trp Gly Pro Asp Gln Lys  
 130 135 140

<210> 121  
 <211> 444  
 <212> DNA  
 <213> Felis catus

<400> 121  
 ttactttctgg tctggtcccc agcagtcaaa ggggttggtta aacagaaaat ccttcagatt 60  
 ctcttttgaaa tttttgaagg tgatagtctg ggtttcacag ggcgtttccg gagtaagggg 120  
 gcagtgctgc ttgtaatggt tggccatcat tctcagaggc tccttgaggc tgatgaggct 180  
 gcccgtagg cctgctcgt acagcttttag gtgagtctgc aggcatctcg gctcctcagg 240  
 gtcaaacatt tcagagacga cttctactgc ttcattcatc acagcagtta tttcactact 300  
 gttgttcaga aggctcaggg cctccttgat ggcattccacg tggtgccagg gccgagtgac 360  
 agagctgggt gaactggtgg gtgcagagat gctgcagacc acagtgccca ggaaaagcag 420  
 gttctgcagc cacatggtgg atcc 444

<210> 122  
<211> 432  
<212> DNA  
<213> Felis catus

<400> 122  
atgtggctgc agaacctgct tttcctgggc actgtggtct gcagcatctc tgcacccacc 60  
agttcaccca gctctgtcac tcggccctgg caacacgtgg atgccatcaa ggaggccctg 120  
agccttctga acaacagtag tgaaataact gctgtgatga atgaagcagt agaagtcgtc 180  
tctgaaatgt ttgaccctga ggagccgaaa tgcctgcaga ctcacctaaa gctgtacgag 240  
cagggcctac ggggcagcct catcagcctc aaggagcctc tgagaatgat ggccaaccat 300  
tacaagcagc actgccccct tactccggaa acgccctgtg aaaccagac tatcaccttc 360  
aaaaatttca aagagaatct gaaggatttt ctgtttaaca acccctttga ctgctgggga 420  
ccagaccaga ag 432

<210> 123  
<211> 432  
<212> DNA  
<213> Felis catus

<400> 123  
cttctggtct ggtccccagc agtcaaaggg gttgttaaac agaaaatcct tcagattctc 60  
tttgaaattt ttgaagggtga tagtctgggt ttcacagggc gtttccggag taagggggca 120  
gtgctgcttg taatggttgg ccatcattct cagaggctcc ttgaggctga tgaggctgcc 180  
ccgtaggccc tgctcgtaca gctttagggt agtctgcagg catttcgggt cctcagggtc 240  
aaacatttca gagacgactt ctactgcttc attcatcaca gcagttatct cactactgtt 300  
gttcagaagg ctcagggcct ccttgatggc atccacgtgt tgccagggcc gagtgacaga 360  
gctgggtgaa ctggtgggtg cagagatgct gcagaccaca gtgcccagga aaagcaggtt 420  
ctgcagccac at 432

<210> 124

<211> 381  
 <212> DNA  
 <213> Felis catus

<220>  
 <221> CDS  
 <222> (1)..(381)

<400> 124  
 gca ccc acc agt tca ccc agc tct gtc act cgg ccc tgg caa cac gtg 48  
 Ala Pro Thr Ser Ser Pro Ser Ser Val Thr Arg Pro Trp Gln His Val  
 1 5 10 15  
 gat gcc atc aag gag gcc ctg agc ctt ctg aac aac agt agt gaa ata 96  
 Asp Ala Ile Lys Glu Ala Leu Ser Leu Leu Asn Asn Ser Ser Glu Ile  
 20 25 30  
 act gct gtg atg aat gaa gca gta gaa gtc gtc tct gaa atg ttt gac 144  
 Thr Ala Val Met Asn Glu Ala Val Glu Val Val Ser Glu Met Phe Asp  
 35 40 45  
 cct gag gag ccg aaa tgc ctg cag act cac cta aag ctg tac gag cag 192  
 Pro Glu Glu Pro Lys Cys Leu Gln Thr His Leu Lys Leu Tyr Glu Gln  
 50 55 60  
 ggc cta cgg ggc agc ctc atc agc ctc aag gag cct ctg aga atg atg 240  
 Gly Leu Arg Gly Ser Leu Ile Ser Leu Lys Glu Pro Leu Arg Met Met  
 65 70 75 80  
 gcc aac cat tac aag cag cac tgc ccc ctt act ccg gaa acg ccc tgt 288  
 Ala Asn His Tyr Lys Gln His Cys Pro Leu Thr Pro Glu Thr Pro Cys  
 85 90 95  
 gaa acc cag act atc acc ttc aaa aat ttc aaa gag aat ctg aag gat 336  
 Glu Thr Gln Thr Ile Thr Phe Lys Asn Phe Lys Glu Asn Leu Lys Asp  
 100 105 110  
 ttt ctg ttt aac aac ccc ttt gac tgc tgg gga cca gac cag aag 381  
 Phe Leu Phe Asn Asn Pro Phe Asp Cys Trp Gly Pro Asp Gln Lys  
 115 120 125

<210> 125  
 <211> 127  
 <212> PRT  
 <213> Felis catus

<400> 125

Ala Pro Thr Ser Ser Pro Ser Ser Val Thr Arg Pro Trp Gln His Val  
 1 5 10 15

Asp Ala Ile Lys Glu Ala Leu Ser Leu Leu Asn Asn Ser Ser Glu Ile  
 20 25 30

Thr Ala Val Met Asn Glu Ala Val Glu Val Val Ser Glu Met Phe Asp  
 35 40 45

Pro Glu Glu Pro Lys Cys Leu Gln Thr His Leu Lys Leu Tyr Glu Gln  
 50 55 60

Gly Leu Arg Gly Ser Leu Ile Ser Leu Lys Glu Pro Leu Arg Met Met  
 65 70 75 80

Ala Asn His Tyr Lys Gln His Cys Pro Leu Thr Pro Glu Thr Pro Cys  
 85 90 95

Glu Thr Gln Thr Ile Thr Phe Lys Asn Phe Lys Glu Asn Leu Lys Asp  
 100 105 110

Phe Leu Phe Asn Asn Pro Phe Asp Cys Trp Gly Pro Asp Gln Lys  
 115 120 125

<210> 126  
 <211> 381  
 <212> DNA  
 <213> Felis catus

<400> 126  
 cttctggtct ggtccccagc agtcaaaggg gttgttaaac agaaaatcct tcagattctc 60  
 tttgaaattt ttgaaggtga tagtctgggt ttcacagggc gtttccggag taagggggca 120  
 gtgctgcttg taatgggttg ccatcattct cagaggctcc ttgaggctga tgaggctgcc 180  
 ccgtaggccc tgctcgta ca gctttaggtg agtctgcagg catttcggct cctcagggtc 240  
 aaacatttca gagacgactt ctactgcttc attcatcaca gcagttatct cactactgtt 300  
 gttcagaagg ctcagggcct ccttgatggc atccacgtgt tgccagggcc gagtgacaga 360  
 gctgggtgaa ctggtgggtg c 381

<210> 127  
 <211> 28



<212> DNA  
<213> Artificial Sequence

<400> 127  
cctcgagatt cagctttcaa tgcctgta

28

<210> 128  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 128  
tgcccrstcg gcttcttctc c

21

<210> 129  
<211> 23  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 129  
cgactctctt trccrtcctc ctg

23

<210> 130  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 130  
cctcaaattg cggcacatgt c

21

<210> 131  
<211> 22

<212> DNA  
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 131  
ctgttcagag tttgagtaag cc

22

<210> 132  
<211> 28  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 132  
gaagatacca tttcaacttt aacacagc

28

<210> 133  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 133  
tgctgtattg tgaagactcc cagc

24

<210> 134  
<211> 16  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 134  
atgcactttc tttgcc

16

<210> 135  
<211> 42  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 135  
ctggaggaaa akacttcrat gattctgata tctgaaatat at

42

<210> 136  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 136  
ctgacycttk sttggsctc attctca

27

<210> 137  
<211> 36  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 137  
gggctcgaga aaagatttgc tgtagaaaat cccatg

36

<210> 138  
<211> 32  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic

Primer

<400> 138

cccgcggcgcg ctcaactttc cgggtgtccac tc

32

<210> 139

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 139

gtcmtggctc tyrcttgccct tgg

23

<210> 140

<211> 23

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 140

aaastgggcy acytcgattt tgg

23

<210> 141

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 141

gtgatgttgm ycagctcctc

20

<210> 142

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 142

aattaaccct cactaaaggg

20

<210> 143

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 143

atggcgctct gggtgactgt

20

<210> 144

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 144

ggcttttgag agcacagtgc

20

<210> 145

<211> 29

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 145

cccatatga gccctgtgac tccctcccc

29

<210> 146  
<211> 30  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 146  
ggggaattct catctgaaat ttccatggcg 30

<210> 147  
<211> 24  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 147  
atggcgctgc cctcttcctt ctg 24

<210> 148  
<211> 28  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 148  
tcatttctcg ctccttaatc ttttctgc 28

<210> 149  
<211> 37  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 149  
cagggatcca ccatgtggct gcagaacctg cttttcc 37

<210> 150  
<211> 50  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 150  
ttacttctgg tctgggtcccc agcagtcaaa ggggttgta aacagaaaat 50

<210> 151  
<211> 18  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 151  
cacagyccca tctcctcc 18

<210> 152  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 152  
gtaatacgac tcactatagg gc 22

<210> 153  
<211> 26  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 153

acggaattcg agatgatagt gctggc

26

<210> 154

<211> 28

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic  
Primer

<400> 154

gtgtctagat ttggtagaaa aggatgat

28

<210> 155

<211> 567

<212> DNA

<213> Felis catus

<220>

<221> CDS

<222> (1)..(567)

<400> 155

atg gcg ctg ccc tct tcc ttc ttg gtg gcc ctg gtg gcg ctg ggc tgc 48  
Met Ala Leu Pro Ser Ser Phe Leu Val Ala Leu Val Ala Leu Gly Cys  
1 5 10 15

aac tcc gtc tgc tct ctg ggc tgt gac ctg cct cag acc cac ggc ctg 96  
Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu  
20 25 30

ctg aac agg agg gcc ttg acg ctc ctg gga caa atg agg aga ctc cct 144  
Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro  
35 40 45

gcc agc tcc tgt cag aag gac aga agt gac ttc gcc ttc ccc cag gac 192  
Ala Ser Ser Cys Gln Lys Asp Arg Ser Asp Phe Ala Phe Pro Gln Asp  
50 55 60



gtg	ttt	ggt	gga	gac	cag	tcc	cac	aag	gcc	caa	gcc	ctc	tcg	gtg	gtg	240
Val	Phe	Gly	Gly	Asp	Gln	Ser	His	Lys	Ala	Gln	Ala	Leu	Ser	Val	Val	
65					70				75						80	

cac	gtg	acg	aac	cag	aag	atc	ttc	cac	ttc	ttc	tgc	aca	gag	gcg	tcc	288
His	Val	Thr	Asn	Gln	Lys	Ile	Phe	His	Phe	Phe	Cys	Thr	Glu	Ala	Ser	
			85					90						95		

tcg	tct	gct	gct	tgg	aac	acc	acc	ctc	ctg	gag	gaa	ttc	tgc	acg	gga	336
Ser	Ser	Ala	Ala	Trp	Asn	Thr	Thr	Leu	Leu	Glu	Glu	Phe	Cys	Thr	Gly	
		100						105					110			

ctt	gat	tgg	cag	ctg	acc	cgc	ctg	gaa	gcc	tgt	gtc	atg	cag	gag	gtg	384
Leu	Asp	Trp	Gln	Leu	Thr	Arg	Leu	Glu	Ala	Cys	Val	Met	Gln	Glu	Val	
	115						120					125				

ggg	gag	gga	gag	gct	ccc	ctc	acg	aac	gag	gac	tcc	atc	ctg	agg	aac	432
Gly	Glu	Gly	Glu	Ala	Pro	Leu	Thr	Asn	Glu	Asp	Ser	Ile	Leu	Arg	Asn	
130						135					140					

tac	ttc	caa	aga	ctc	tcc	ctc	tac	ctg	caa	gag	aag	aaa	tac	agc	cct	480
Tyr	Phe	Gln	Arg	Leu	Ser	Leu	Tyr	Leu	Gln	Glu	Lys	Lys	Tyr	Ser	Pro	
145					150				155						160	

tgt	gcc	tgg	gag	atc	gtc	aga	gca	gaa	atc	atg	aga	tcc	ttg	tat	tat	528
Cys	Ala	Trp	Glu	Ile	Val	Arg	Ala	Glu	Ile	Met	Arg	Ser	Leu	Tyr	Tyr	
			165					170						175		

tca	tca	aca	gcc	ttg	cag	aaa	aga	tta	agg	agc	gag	aaa				567
Ser	Ser	Thr	Ala	Leu	Gln	Lys	Arg	Leu	Arg	Ser	Glu	Lys				
			180					185								

<210> 156  
 <211> 189  
 <212> PRT  
 <213> Felis catus

<400> 156																
Met	Ala	Leu	Pro	Ser	Ser	Phe	Leu	Val	Ala	Leu	Val	Ala	Leu	Gly	Cys	
1				5					10					15		
Asn	Ser	Val	Cys	Ser	Leu	Gly	Cys	Asp	Leu	Pro	Gln	Thr	His	Gly	Leu	
			20					25					30			
Leu	Asn	Arg	Arg	Ala	Leu	Thr	Leu	Leu	Gly	Gln	Met	Arg	Arg	Leu	Pro	
	35						40					45				

Ala Ser Ser Cys Gln Lys Asp Arg Ser Asp Phe Ala Phe Pro Gln Asp  
 50 55 60

Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val  
 65 70 75 80

His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser  
 85 90 95

Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly  
 100 105 110

Leu Asp Trp Gln Leu Thr Arg Leu Glu Ala Cys Val Met Gln Glu Val  
 115 120 125

Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ser Ile Leu Arg Asn  
 130 135 140

Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro  
 145 150 155 160

Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr  
 165 170 175

Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys  
 180 185

<210> 157  
 <211> 567  
 <212> DNA  
 <213> Felis catus

<400> 157  
 tttctcgctc cttaatcttt tctgcaaggc tgttgatgaa taatacaagg atctcatgat 60  
 ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagaggga 120  
 gagtcttttg aagtagttcc tcaggatgga gtcctcgttc gtgaggggag cctctccctc 180  
 cccacctcc tgcattgacac aggcttccag gcgggtcagc tgccaatcaa gtcccgtgca 240  
 gaattcctcc aggaggggtg tgttccaagc agcagacgag gacgcctctg tgcagaagaa 300  
 gtggaagatc ttctgggttcg tcacgtgcac caccgagagg gcttgggcct tgtgggactg 360  
 gtctccacca aacacgtcct gggggaaggc gaagtcactt ctgtccttct gacaggagct 420

ggcagggagt ctctcattt gtcccaggag cgtcaaggcc ctctgttca gcaggccgtg 480  
 ggtctgaggc aggtcacagc ccagagagca gacggagttg cagcccagcg ccaccagggc 540  
 caccaagaag gaagagggca ggcgcat 567

<210> 158  
 <211> 498  
 <212> DNA  
 <213> Felis catus

<220>  
 <221> CDS  
 <222> (1)..(498)

<400> 158  
 tgt gac ctg cct cag acc cac ggc ctg ctg aac agg agg gcc ttg acg 48  
 Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr  
 1 5 10 15  
 ctc ctg gga caa atg agg aga ctc cct gcc agc tcc tgt cag aag gac 96  
 Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp  
 20 25 30  
 aga agt gac ttc gcc ttc ccc cag gac gtg ttt ggt gga gac cag tcc 144  
 Arg Ser Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser  
 35 40 45  
 cac aag gcc caa gcc ctc tcg gtg gtg cac gtg acg aac cag aag atc 192  
 His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile  
 50 55 60  
 ttc cac ttc ttc tgc aca gag gcg tcc tcg tct gct gct tgg aac acc 240  
 Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr  
 65 70 75 80  
 acc ctc ctg gag gaa ttc tgc acg gga ctt gat tgg cag ctg acc cgc 288  
 Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Trp Gln Leu Thr Arg  
 85 90 95  
 ctg gaa gcc tgt gtc atg cag gag gtg ggg gag gga gag gct ccc ctc 336  
 Leu Glu Ala Cys Val Met Gln Glu Val Gly Glu Gly Glu Ala Pro Leu  
 100 105 110  
 acg aac gag gac tcc atc ctg agg aac tac ttc caa aga ctc tcc ctc 384  
 Thr Asn Glu Asp Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu  
 115 120 125

tac ctg caa gag aag aaa tac agc cct tgt gcc tgg gag atc gtc aga 432  
Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg  
130 135 140

gca gaa atc atg aga tcc ttg tat tat tca tca aca gcc ttg cag aaa 480  
Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys  
145 150 155 160

aga tta agg agc gag aaa 498  
Arg Leu Arg Ser Glu Lys  
165

<210> 159  
<211> 166  
<212> PRT  
<213> Felis catus

<400> 159  
Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr  
1 5 10 15

Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp  
20 25 30

Arg Ser Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser  
35 40 45

His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile  
50 55 60

Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr  
65 70 75 80

Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Trp Gln Leu Thr Arg  
85 90 95

Leu Glu Ala Cys Val Met Gln Glu Val Gly Glu Gly Glu Ala Pro Leu  
100 105 110

Thr Asn Glu Asp Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu  
115 120 125

Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg  
130 135 140

Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys

145

150

155

160

Arg Leu Arg Ser Glu Lys  
165

&lt;210&gt; 160

&lt;211&gt; 498

&lt;212&gt; DNA

&lt;213&gt; Felis catus

&lt;400&gt; 160

tttctcgctc cttaatcttt tctgcaaggc tgttgatgaa taatacaagg atctcatgat 60

ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagaggga 120

gagtcttttg aagtagttcc tcaggatgga gtcctcggtc gtgaggggag cctctccctc 180

ccccacctcc tgcatgacac aggcttccag gcgggtcagc tgccaatcaa gtcccgtgca 240

gaattcctcc aggaggggtgg tgttccaagc agcagacgag gacgcctctg tgcagaagaa 300

gtggaagatc ttctgggttcg tcacgtgcac caccgagagg gcttggggcct tgtgggactg 360

gtctccacca aacacgtcct gggggaaggc gaagtcactt ctgtccttct gacaggagct 420

ggcagggagt ctctcatctt gtcccaggag cgtcaaggcc ctctgtttca gcaggccgtg 480

ggtctgaggc aggtcaca 498

&lt;210&gt; 161

&lt;211&gt; 582

&lt;212&gt; DNA

&lt;213&gt; Felis catus

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (1)..(582)

&lt;400&gt; 161

atg gcg ctg ccc tct tcc ttc ttg gtg gcc ctg gtg gcg ctg ggc tgc 48  
Met Ala Leu Pro Ser Ser Phe Leu Val Ala Leu Val Ala Leu Gly Cys  
1 5 10 15

aac tcc gtc tgc tct ctg ggc tgt gat ctg cct cag acc cac ggc ctg 96  
Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu  
20 25 30

ctg aac agg agg gcc ttg acg ctc ctg gga caa atg agg aga ctc cct	144
Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro	
35 40 45	
gcc agc tcc tgt cag aag gac aga agt gac ttc gcc ttc ccc cag gac	192
Ala Ser Ser Cys Gln Lys Asp Arg Ser Asp Phe Ala Phe Pro Gln Asp	
50 55 60	
gtg ttc ggt gga gac cag tcc cac aag gcc caa gcc ctc tcg gtg gtg	240
Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val	
65 70 75 80	
cac gtg acg aac cag aag atc ttc cac ttc ttc tgc aca gag gcg tcc	288
His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser	
85 90 95	
tcg tct gct gct tgg aac acc acc ctc ctg gag gaa ttc tgc acg gga	336
Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly	
100 105 110	
ctt gat cgg cag ctg acc cgc ctg gaa gcc tgt gtc gtg cag gag gtg	384
Leu Asp Arg Gln Leu Thr Arg Leu Glu Ala Cys Val Val Gln Glu Val	
115 120 125	
ggg gag gga gag gct ccc ctg acg aac gag gac att cat ccc gag gac	432
Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ile His Pro Glu Asp	
130 135 140	
tcc atc ctg agg aac tac ttc caa aga ctc tcc ctc tac ctg caa gag	480
Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu	
145 150 155 160	
aag aaa tac agc cct tgt gcc tgg gag atc gtc aga gca gaa atc atg	528
Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met	
165 170 175	
aga tcc ttg tat tat tca tca aca gcc ttg cag aaa aga tta agg agc	576
Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser	
180 185 190	
gag aaa	582
Glu Lys	

<210> 162  
 <211> 194  
 <212> PRT

<213> Felis catus

<400> 162

Met Ala Leu Pro Ser Ser Phe Leu Val Ala Leu Val Ala Leu Gly Cys  
1 5 10 15

Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu  
20 25 30

Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro  
35 40 45

Ala Ser Ser Cys Gln Lys Asp Arg Ser Asp Phe Ala Phe Pro Gln Asp  
50 55 60

Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val  
65 70 75 80

His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser  
85 90 95

Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly  
100 105 110

Leu Asp Arg Gln Leu Thr Arg Leu Glu Ala Cys Val Val Gln Glu Val  
115 120 125

Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ile His Pro Glu Asp  
130 135 140

Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu  
145 150 155 160

Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met  
165 170 175

Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser  
180 185 190

Glu Lys

<210> 163

<211> 582

<212> DNA

<213> Felis catus

<400> 163

tttctcgctc cttaatcttt tctgcaaggc tgttgatgaa taatacaagg atctcatgat 60  
ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagaggga 120  
gagtctttgg aagtagttcc tcaggatgga gtcctcgga tgaatgtcct cgttcgtcag 180  
gggagcctct ccctccccca cctcctgcac gacacaggct tccaggcggg tcagctgccg 240  
atcaagtccc gtgcagaatt cctccaggag ggtgggtgttc caagcagcag acgaggacgc 300  
ctctgtgcag aagaagtgga agatcttctg gttcgtcacg tgcaccaccg agagggcttg 360  
ggccttgtgg gactgggtctc caccgaacac gtcctggggg aaggcgaagt cacttctgtc 420  
cttctgacag gagctggcag ggagtctcct catttgtccc aggagcgtca aggccctcct 480  
gttcagcagg ccgtgggtct gaggcagatc acagcccaga gagcagacgg agttgcagcc 540  
cagcgccacc agggccacca agaaggaaga gggcagcgcc at 582

<210> 164

<211> 513

<212> DNA

<213> Felis catus

<220>

<221> CDS

<222> (1)..(513)

<400> 164

tgt	gat	ctg	cct	cag	acc	cac	ggc	ctg	ctg	aac	agg	agg	gcc	ttg	acg	48
Cys	Asp	Leu	Pro	Gln	Thr	His	Gly	Leu	Leu	Asn	Arg	Arg	Ala	Leu	Thr	
1				5				10					15			
ctc	ctg	gga	caa	atg	agg	aga	ctc	cct	gcc	agc	tcc	tgt	cag	aag	gac	96
Leu	Leu	Gly	Gln	Met	Arg	Arg	Leu	Pro	Ala	Ser	Ser	Cys	Gln	Lys	Asp	
			20					25					30			
aga	agt	gac	ttc	gcc	ttc	ccc	cag	gac	gtg	ttc	ggg	gga	gac	cag	tcc	144
Arg	Ser	Asp	Phe	Ala	Phe	Pro	Gln	Asp	Val	Phe	Gly	Gly	Asp	Gln	Ser	
			35				40					45				
cac	aag	gcc	caa	gcc	ctc	tcg	gtg	gtg	cac	gtg	acg	aac	cag	aag	atc	192
His	Lys	Ala	Gln	Ala	Leu	Ser	Val	Val	His	Val	Thr	Asn	Gln	Lys	Ile	
			50				55				60					



ttc cac ttc ttc tgc aca gag gcg tcc tcg tct gct gct tgg aac acc 240  
Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr  
65 70 75 80

acc ctc ctg gag gaa ttc tgc acg gga ctt gat cgg cag ctg acc cgc 288  
Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Arg Gln Leu Thr Arg  
85 90 95

ctg gaa gcc tgt gtc gtg cag gag gtg ggg gag gga gag gct ccc ctg 336  
Leu Glu Ala Cys Val Val Gln Glu Val Gly Glu Gly Glu Ala Pro Leu  
100 105 110

acg aac gag gac att cat ccc gag gac tcc atc ctg agg aac tac ttc 384  
Thr Asn Glu Asp Ile His Pro Glu Asp Ser Ile Leu Arg Asn Tyr Phe  
115 120 125

caa aga ctc tcc ctc tac ctg caa gag aag aaa tac agc cct tgt gcc 432  
Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala  
130 135 140

tgg gag atc gtc aga gca gaa atc atg aga tcc ttg tat tat tca tca 480  
Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser  
145 150 155 160

aca gcc ttg cag aaa aga tta agg agc gag aaa 513  
Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys  
165 170

<210> 165  
<211> 171  
<212> PRT  
<213> Felis catus

<400> 165  
Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr  
1 5 10 15

Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp  
20 25 30

Arg Ser Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser  
35 40 45

His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile  
50 55 60

Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr

65		70		75		80									
Thr	Leu	Leu	Glu	Glu	Phe	Cys	Thr	Gly	Leu	Asp	Arg	Gln	Leu	Thr	Arg
			85					90					95		
Leu	Glu	Ala	Cys	Val	Val	Gln	Glu	Val	Gly	Glu	Gly	Glu	Ala	Pro	Leu
		100					105						110		
Thr	Asn	Glu	Asp	Ile	His	Pro	Glu	Asp	Ser	Ile	Leu	Arg	Asn	Tyr	Phe
	115						120					125			
Gln	Arg	Leu	Ser	Leu	Tyr	Leu	Gln	Glu	Lys	Lys	Tyr	Ser	Pro	Cys	Ala
	130						135				140				
Trp	Glu	Ile	Val	Arg	Ala	Glu	Ile	Met	Arg	Ser	Leu	Tyr	Tyr	Ser	Ser
145					150					155					160
Thr	Ala	Leu	Gln	Lys	Arg	Leu	Arg	Ser	Glu	Lys					
			165						170						

<210> 166  
 <211> 513  
 <212> DNA  
 <213> Felis catus

<400> 166  
 tttctcgctc cttaatcttt tctgcaaggc tgttgatgaa taatacaagg atctcatgat 60  
 ttctgctctg acgatctccc aggcacaagg gctgtatttc ttctcttgca ggtagaggga 120  
 gagtctttgg aagtagttcc tcaggatgga gtcctcggga tgaatgtcct cgttcgtcag 180  
 gggagcctct ccctccccca cctcctgcac gacacaggct tccaggcggg tcagctgccg 240  
 atcaagtccc gtgcagaatt cctccaggag ggtggtgttc caagcagcag acgaggacgc 300  
 ctctgtgcag aagaagtgga agatcttctg gttcgtcacg tgcaccaccg agagggcttg 360  
 ggccttgtgg gactggtctc caccgaacac gtccctggggg aaggcgaagt cacttctgtc 420  
 cttctgacag gagctggcag ggagtctcct catttgtccc aggagcgtca aggccctcct 480  
 gttcagcagg ccgtgggtct gaggcagatc aca 513

<210> 167  
 <211> 567

<212> DNA  
 <213> Felis catus

<220>  
 <221> CDS  
 <222> (1)..(567)

<400> 167

atg gcg ctg ccc tct tcc ttc ttg gtg gcc ctg gtg gcg ctg ggc tgc	48
Met Ala Leu Pro Ser Ser Phe Leu Val Ala Leu Val Ala Leu Gly Cys	
1 5 10 15	
aac tct gtc tgc tct ctg ggc tgt gac ctg cct cag acc cac ggc ctg	96
Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu	
20 25 30	
ctg aac agg agg gcc ttg acg ctc ctg gga caa atg agg aga ctc cct	144
Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro	
35 40 45	
gcc agc tcc tgc cag aag gac aga aat gac ttc gcc ttc ccc cag gac	192
Ala Ser Ser Cys Gln Lys Asp Arg Asn Asp Phe Ala Phe Pro Gln Asp	
50 55 60	
gtg ttc ggt gga gac cag tcc cac aag gcc caa gcc ctc tcg gtg gtg	240
Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val	
65 70 75 80	
cac gtg acg aac cag aag atc ttc cac ttc ttc tgc aca gag gcg tcc	288
His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser	
85 90 95	
tcg tct gct gct tgg aac acc acc ctc ctg gag gaa ttc tgc acg gga	336
Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly	
100 105 110	
ctt gat cgg cag ctg acc cgc ctg gaa gcc tgt gtc gtg cag gag gtg	384
Leu Asp Arg Gln Leu Thr Arg Leu Glu Ala Cys Val Val Gln Glu Val	
115 120 125	
ggg gag gga gag gct ccc ctc acg aac gag gac tcc atc ctg agg aac	432
Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ser Ile Leu Arg Asn	
130 135 140	
tac ttc caa aga ctc tcc ctc tac ctg caa gag aag aaa tac agc cct	480
Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro	
145 150 155 160	

tgt gcc tgg gag atc gtc aga gca gaa atc atg aga tcc ttg tat tat 528  
 Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr  
                   165                  170                  175

tca tca aca gcc ttg cag aaa aga tta agg agc gag aaa 567  
 Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys  
                   180                  185

<210> 168  
 <211> 189  
 <212> PRT  
 <213> Felis catus

<400> 168  
 Met Ala Leu Pro Ser Ser Phe Leu Val Ala Leu Val Ala Leu Gly Cys  
       1                  5                  10                  15

Asn Ser Val Cys Ser Leu Gly Cys Asp Leu Pro Gln Thr His Gly Leu  
                   20                  25                  30

Leu Asn Arg Arg Ala Leu Thr Leu Leu Gly Gln Met Arg Arg Leu Pro  
                   35                  40                  45

Ala Ser Ser Cys Gln Lys Asp Arg Asn Asp Phe Ala Phe Pro Gln Asp  
                   50                  55                  60

Val Phe Gly Gly Asp Gln Ser His Lys Ala Gln Ala Leu Ser Val Val  
       65                  70                  75                  80

His Val Thr Asn Gln Lys Ile Phe His Phe Phe Cys Thr Glu Ala Ser  
                   85                  90                  95

Ser Ser Ala Ala Trp Asn Thr Thr Leu Leu Glu Glu Phe Cys Thr Gly  
                   100                  105                  110

Leu Asp Arg Gln Leu Thr Arg Leu Glu Ala Cys Val Val Gln Glu Val  
                   115                  120                  125

Gly Glu Gly Glu Ala Pro Leu Thr Asn Glu Asp Ser Ile Leu Arg Asn  
                   130                  135                  140

Tyr Phe Gln Arg Leu Ser Leu Tyr Leu Gln Glu Lys Lys Tyr Ser Pro  
       145                  150                  155                  160

Cys Ala Trp Glu Ile Val Arg Ala Glu Ile Met Arg Ser Leu Tyr Tyr  
                   165                  170                  175

Ser Ser Thr Ala Leu Gln Lys Arg Leu Arg Ser Glu Lys  
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 <211> 567  
 <212> DNA  
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<400> 169  
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 gagtcttttg aagtagttcc tcaggatgga gtcctcggtc gtgaggggag cctctccctc 180  
 cccacactcc tgcacgacac aggcttcag gcggtcagc tgccgatcaa gtcccgtgca 240  
 gaattcctcc aggaggggtg tgttccaagc agcagacgag gacgcctctg tgcagaagaa 300  
 gtggaagatc ttctgggttcg tcacgtgcac caccgagagg gcttgggcct tgtgggactg 360  
 gtctccaccg aacacgtcct gggggaaggc gaagtcattt ctgtccttct ggcaggagct 420  
 ggcagggagt ctctcattt gtcccaggag cgtcaaggcc ctctgttca gcaggccgtg 480  
 ggtctgaggc aggtcacagc ccagagagca gacagagttg cagcccagcg ccaccagggc 540  
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<210> 170  
 <211> 498  
 <212> DNA  
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<220>  
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<400> 170  
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 Cys Asp Leu Pro Gln Thr His Gly Leu Leu Asn Arg Arg Ala Leu Thr  
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 ctc ctg gga caa atg agg aga ctc cct gcc agc tcc tgc cag aag gac 96  
 Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp  
 20 25 30

aga aat gac ttc gcc ttc ccc cag gac gtg ttc ggt gga gac cag tcc	144
Arg Asn Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser	
35 40 45	
 cac aag gcc caa gcc ctc tcg gtg gtg cac gtg acg aac cag aag atc	192
His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile	
50 55 60	
 ttc cac ttc ttc tgc aca gag gcg tcc tcg tct gct gct tgg aac acc	240
Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr	
65 70 75 80	
 acc ctc ctg gag gaa ttc tgc acg gga ctt gat cgg cag ctg acc cgc	288
Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Arg Gln Leu Thr Arg	
85 90 95	
 ctg gaa gcc tgt gtc gtg cag gag gtg ggg gag gga gag gct ccc ctc	336
Leu Glu Ala Cys Val Val Gln Glu Val Gly Glu Gly Glu Ala Pro Leu	
100 105 110	
 acg aac gag gac tcc atc ctg agg aac tac ttc caa aga ctc tcc ctc	384
Thr Asn Glu Asp Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu	
115 120 125	
 tac ctg caa gag aag aaa tac agc cct tgt gcc tgg gag atc gtc aga	432
Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg	
130 135 140	
 gca gaa atc atg aga tcc ttg tat tat tca tca aca gcc ttg cag aaa	480
Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys	
145 150 155 160	
 aga tta agg agc gag aaa	498
Arg Leu Arg Ser Glu Lys	
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<210> 171  
 <211> 166  
 <212> PRT  
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<400> 171  
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Leu Leu Gly Gln Met Arg Arg Leu Pro Ala Ser Ser Cys Gln Lys Asp

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 Arg Asn Asp Phe Ala Phe Pro Gln Asp Val Phe Gly Gly Asp Gln Ser  
 35 40 45  
 His Lys Ala Gln Ala Leu Ser Val Val His Val Thr Asn Gln Lys Ile  
 50 55 60  
 Phe His Phe Phe Cys Thr Glu Ala Ser Ser Ser Ala Ala Trp Asn Thr  
 65 70 75 80  
 Thr Leu Leu Glu Glu Phe Cys Thr Gly Leu Asp Arg Gln Leu Thr Arg  
 85 90 95  
 Leu Glu Ala Cys Val Val Gln Glu Val Gly Glu Gly Glu Ala Pro Leu  
 100 105 110  
 Thr Asn Glu Asp Ser Ile Leu Arg Asn Tyr Phe Gln Arg Leu Ser Leu  
 115 120 125  
 Tyr Leu Gln Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Ile Val Arg  
 130 135 140  
 Ala Glu Ile Met Arg Ser Leu Tyr Tyr Ser Ser Thr Ala Leu Gln Lys  
 145 150 155 160  
 Arg Leu Arg Ser Glu Lys  
 165

<210> 172  
 <211> 498  
 <212> DNA  
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<400> 172  
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 gagtctttgg aagtagttcc tcaggatgga gtccctcggtc gtgaggggag cctctccctc 180  
 cccacctcc tgcacgacac aggcctccag gcgggtcagc tgccgatcaa gtcccgtgca 240  
 gaattcctcc aggaggggtgg tgttccaagc agcagacgag gacgcctctg tgcagaagaa 300  
 gtggaagatc ttctggttcg tcacgtgcac caccgagagg gcttgggcct tgtgggactg 360

gtctccaccg aacacgtcct gggggaaggc gaagtcattt ctgtccttct ggcaggagct 420  
 ggcagggagt ctcctcattt gtcccaggag cgtcaaggcc ctcctgttca gcaggccgtg 480  
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<210> 173  
 <211> 29  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic  
 Primer

<400> 173  
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<210> 174  
 <211> 40  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic  
 Primer

<400> 174  
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